COMPARATIVE EVALUATION OF TRANSPULMONARY PRESSURE GUIDED VENTILATION VERSUS CONVENTIONAL VENTILATION IN PATIENTS WITH ARDS

A THESIS SUBMITTED TO

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT (PUNJAB)

IN THE PARTIAL FULFILLMENT

FOR THE AWARD OF DEGREE OF

DOCTORATE OF MEDICINE

IN

CRITICAL CARE MEDICINE

MAY 2022

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Dedicated

to

my Family

&

Teachers

ACKNOWLEDGEMENT

To put emotions on paper is an incredibly difficult task. Words perhaps would fail to express my deep sense of gratitude and indebtedness to my esteemed teacher **Dr. P.L. Gautam,** my H.O.D. and guide, department of Critical Care Medicine, Dayanand medical college and Hospital, Ludhiana for his encouragement and continuous support in carrying out this whole study at each and every step.

I am extremely thankful to **Dr. Gunchan Paul**, my co-guide, associate professor, department of Critical Care Medicine, Dayanand medical college and Hospital, Ludhiana for her continuous support and encouragement in carrying out the thesis.

I appreciate the help of our **Technical staff** for their help and support throughout.

However, I shall not be able to put into words my appreciation for my family and friends who are close to my heart as without their moral support it would not be possible for me to complete this thesis.

My sincere thanks to all the patients who participated in this study as without their consent, this study would not have reached its destination.

In the end, I express my gratitude to the Almighty God for helping me in each and every step of my life.

Dr. M. RAVI KRISHNA

LIST OF ABBREVIATIONS

ARDS	–	Acute respiratory distress syndrome
COVID -19	–	SARS-CoV-2 virus
C-ARDS	–	Covid- 19 Acute respiratory distress syndrome
CI	–	confidence interval
CPAP	–	continuous positive airway pressure
COMP	–	compliance of respiratory system
Crs	–	respiratory system compliance
CT	–	Computed tomography
ΔPaw	–	change in airway opening pressure
ΔPes	–	change in esophageal pressure
DP	–	Driving pressure
$ECCO_2$	–	extracorporeal CO2 removal
ECMO	–	extracorporeal membrane oxygenation
EELV	–	end-expiratory lung volume
El	–	Elastance of lungs
Elspec	–	specific elastance of the lung
Ers	–	respiratory system elastance
FRC	–	functional residual capacity
FiO_2	–	fraction of inspired oxygen
H type	–	high elastance phenotype
ICU	–	intensive care unit
L type	–	low elastance phenotype
MV	–	mechanical ventilation
MAP	–	mean airway pressure
NO	–	nitric oxide
Pao	–	airway opening pressure
Pab	–	Abdominal pressure
Palv	–	alveolar pressure
Paw	–	airway pressure
Pbs	–	body surface pressure
PBW	–	predicted body weight

Pcw	–	pressure applied on the chest wall
PCV-VG	–	pressure control ventilation- volume guaranteed
PEEP	–	positive end expiratory pressure
PEEPtot	–	PEEP Total
Pel	–	elastic recoil pressure
Pes	–	Esophageal pressure
PFO	–	Patent foramen ovale
Pin	–	inertial pressure
PIP	–	peak inspiratory pressure
Pl/PTP	–	transpulmonary pressure
PM	–	pneumomediastinum
Pmus	–	muscle pressure
Ppl	–	pleural pressure
Pplat	–	plateau pressure
Pres	–	flow-resistive pressure
Ptp	–	transpulmonary pressure
Ptx	–	pneumothorax
Pvent	–	ventilator pressure
pvO2	–	venous partial pressure of oxygen
Qs	–	blood flow through shunt
Qt	–	blood flow through cardiac output
RER	–	Respiratory exchange ratio
R.A.S.S.	–	Richmond Agitation Sedation Scale
Rrs	–	respiratory system resistance
TPP	–	transpulmonary pressure
V/Q	–	ventilation/ perfusion
Va	–	alveolar volume
VCO2	–	CO2 production per minute
Vd	–	dead space volume
Vd/Vt	–	dead space volume/ tidal volume
VILI	–	ventilator induced lung injury
VO2	–	oxygen consumption per minute

ABSTRACT

BACKGROUND: The acute respiratory distress syndrome (ARDS) is a common feature of respiratory failure in critically ill patients with mortality reaching upto 50%. The optimal ventilator strategy and optimal PEEP for treating ARDS has been an issue of concern.

AIMS AND OBJECTIVES: The objective of this study was to analyse if a transpulmonary guided ventilation strategy leads to improvements in oxygenation, respiratory mechanics,CO_2 exchange and VILI.

MATERIALS AND METHODS: We conducted an institutional and prospective study in a tertiary care hospital for a duration of 1 year from April 2020 to April 2021. We enrolled 100 patients of moderate to severe ARDS patients. Patients were randomly allocated into two groups. One group received transpulmonary pressure guided ventilation while the other received conventional ventilation for 12 hours. Measurements were taken at baseline, 6 hours and 12 hours.

RESULTS: Transpulmonary pressure guided ventilation lead to a slight improvement in paO_2/fiO_2(14.34 vs 13.48), and a/A (0.03 vs 0.02) ratios in the intervention group but these values were not statistically significant. Transpulmonary pressure guided ventilation lead to improvement in CO_2 exchange in the intervention group (-7.6 vs. -0.2) which was statistically significant. On further analysis, it was also found that Transpulmonary pressure guided ventilation led to lower driving pressures compared to airway driving pressures which were statistically significant. Transpulmonary pressure guided ventilation group had lower frequency of VILI as compared to conventional group although it was statistically not significant.

CONCLUSION: Transpulmonary pressure guided ventilation can be used to lower airway driving pressures, thus may reduce VILI while maintaining gas exchange.

KEYWORDS: ARDS, VILI, transpulmonary pressure, esophageal pressures, PEEP

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INTRODUCTION

The acute respiratory distress syndrome (ARDS) is a common feature of respiratory failure in critically ill patients. ARDS occurs most often in the setting of pneumonia, sepsis, trauma and is present in roughly 10% of ICU patients and mortality reaching up to 50% in the severe forms of the disease.[1,2]

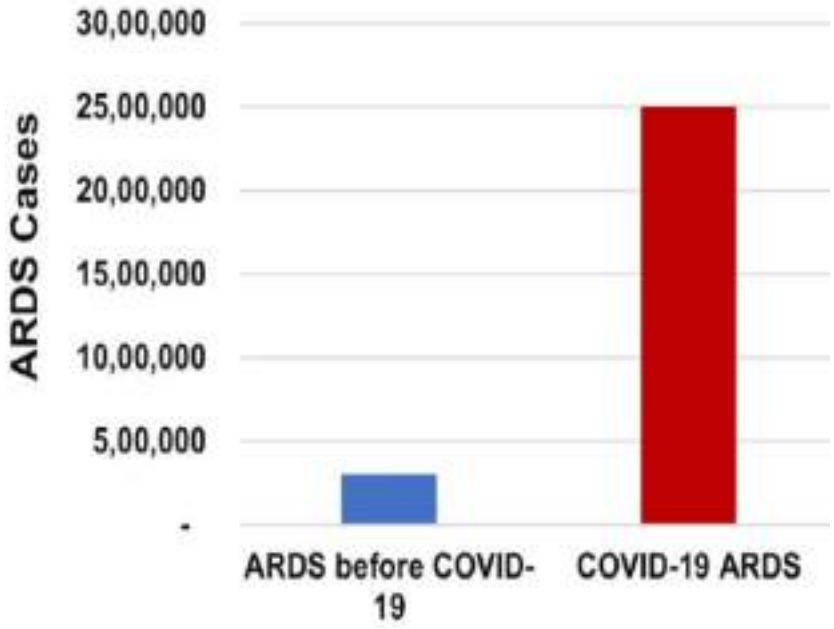
History of ARDS:

Despite being rejected from many prestigious journals, the first description of ARDS by David Ashbaugh was finally published in 1967.[3] That series of 12 patients contained many observations that were further validated in the subsequent decades of research including the description of the disease, major and minor risk factors, pathological findings, the effectiveness of PEEP (positive end-expiratory pressure) at improving oxygenation, and the mixed effectiveness of corticosteroids, diuretics.

Since its description, no other intensive care syndrome has been as extensively studied as acute respiratory distress syndrome. Despite this extensive body of research, there have been only a few treatments that had proven efficacy. Identification of sub phenotypes which would benefit from personalized treatment still eludes physicians.[4]

A small benefit of the current devastating COVID-19 epidemic was the opportunity for studying treatment effects in a large population of patients with viral pneumonia as a shared risk factor for ARDS. These waves of respiratory viral infection have dramatically increased the incidence of ARDS.

FIG. 1 ESTIMATED INCIDENCE OF ARDS BEFORE AND DURING THE COVID-19 PANDEMIC IN THE USA[5]



Since ARDS net study in 2000 ventilator management for patients with acute respiratory distress syndrome (ARDS) was mainly low tidal volume and high PEEP with the maintenance of low plateau pressures.[6] Although low tidal volume ventilation with low plateau pressures appears to be beneficial and lung-protective, optimal management of positive end-expiratory pressure (PEEP) was uncertain especially in the setting of altered chest wall compliance conditions like obesity, ascites etc. Higher levels of PEEP have been shown to be protective in numerous animal experiments but have only shown equivocal benefit in human clinical trials.

Lung inflation reflects transpulmonary pressure (P_{TP}), the difference between pressures at the airway opening and the pleural space (P_{TP}=airway pressure−pleural pressure). This would be a satisfactory strategy if pleural pressure values were predictable or restricted to a narrow range. However, there is evidence that pleural pressure varies widely and unpredictably among patients with ARDS, likely due to factors such as obesity, abdominal fluid accumulation and oedema,

which influence the mechanical behaviour of the chest wall and diaphragm.

Recent trials have shown that mortality correlates more with driving pressure rather than PEEP. We hypothesize that TPP guided PEEP while improving oxygenation and respiratory mechanics minimizes complication rates. Thus we propose this study to test the effects of transpulmonary pressure guided ventilation on oxygenation, CO_2 exchange and also respiratory mechanics and also whether maintaining low driving pressure results in low VILI events as shown in other trials.[7]

AIMS AND OBJECTIVES

- To test that adjusting driving pressure to achieve positive transpulmonary values will lead to improvement in oxygenation and CO_2 exchange.
- To compare Transpulmonary pressure guided ventilation and conventional ventilatory strategies for improvement in oxygenation.
- To compare Transpulmonary pressure guided ventilation and conventional ventilatory strategies for improvement in CO_2 exchange, respiratory system compliance, plateau and peak inspiratory pressures.

REVIEW OF LITERATURE

ARDS is a highly heterogeneous life-threatening severe form of acute respiratory failure. It is characterized by an acute onset of hypoxemia refractory to oxygen treatment and the presence of bilateral pulmonary infiltrates on chest radiograph; without mechanical ventilation, most patients would die. The mortality rate from acute lung injury and the acute respiratory distress syndrome is approximately 24 to 60 percent depending on age.[5]

Since its first description in 1967[8], there have been a large number of studies addressing various clinical aspects of the syndrome (risk factors, epidemiology, treatment) as well as studies addressing its pathogenesis (underlying mechanisms, biomarkers, genetic predisposition). However, despite this intense research activity, there are very few effective therapies for ARDS other than the use of lung protection strategies.

TABLE 1. BERLIN DEFINITION OF ARDS

THE BERLIN DEFINITION OF ACUTE RESPIRATORY DISTRESS SYNDROME[9]	
TIMING:	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
CHEST IMAGING:	Bilateral opacities — not fully explained by effusions, lobar/lung collapse, or nodules
ORIGIN OF EDEMA:	Respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present
OXYGENATION	
Mild:	200 mmHg < PaO_2/FIO_2 ≤300 mmHg with PEEP or CPAP ≥5 cm of H_2O
Moderate:	100 mmHg < PaO_2/FIO_2 ≤200 mmHg with PEEP ≥5 cmH_2O
Severe:	PaO_2/FIO_2 ≤100 mmHg with PEEP ≥5 cmH_2O

PATHOPHYSIOLOGY OF GAS EXCHANGE IN ARDS:

Hypoxemia and impaired CO_2 clearance are characteristic features of ARDS. As the gas exchange is the main physiological abnormality assessed by the physician, understanding the various complex factors at play remains a cornerstone in the management of ARDS.

TABLE 2. MAIN PATHOPHYSIOLOGICAL MECHANISMS OF IMPAIRED GAS EXCHANGE IN ARDS

DISTURBANCE	MAIN MECHANISM
Hypoxemia	Qs/Qt Low V/Q Low PvO_2 Intracardiac shunt
Hypercapnia	Increased Vd/Vt Inhomogenous distribution of ventilation (high V/Q) Increased VCO_2

The concept of V/Q ratio implies that optimal normal gas exchange is essential and that an imbalance in this global/regional ratio is one of the reasons for abnormal gas exchange. Low V/Q ratios (i.e., lung regions where perfusion markedly exceeds ventilation) induce hypoxemia and high V/Q ratio (i.e., lung regions where ventilation markedly exceeds perfusion) induce hypercapnia. Impaired diffusion can be another possible mechanism at the blood-gas interface. However, in the ventilated areas in ARDS, because of the high diffusion coefficient of CO_2 and increased O_2 diffusion gradient induced by the high FiO_2, equilibration of gas partial pressures is usually complete in a functional gas exchange unit.

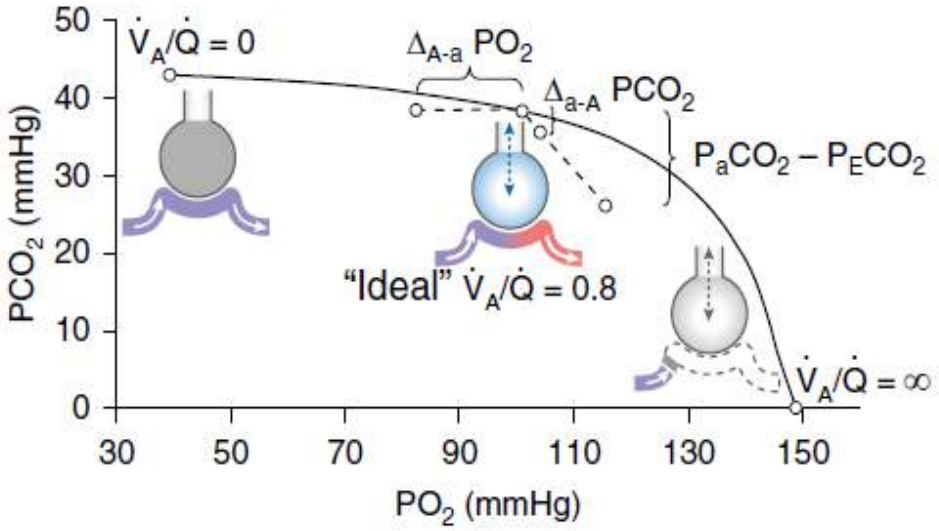
To describe the ideal alveolar air and analyze ventilation-perfusion relationships in the lungs, Riley and Cournand described a simple model with three compartments (normal ratio [i.e., V/Q: = RER], shunt [i.e., V/Q = 0], and dead space [i.e., V/Q = ∞), Increasing the V/Q ratio

by increasing minute ventilation cannot compensate for this effect because of the relatively small contribution to Q of lung regions where ventilation markedly exceeds perfusion.

Therefore, impaired diffusion across the gas–blood barrier does not appear to play any role in gas exchange abnormalities in ARDS. Therefore, for a given FiO_2, total cardiac output, Hb concentration, and respiratory exchange ratio (RER; the ratio of whole-body CO_2 production to O_2 consumption, VCO_2/VO_2, usually of 0.8 at rest with a normal diet), impaired gas exchange is explained by an altered distribution of alveolar ventilation and perfusion (V/Q).

A P(A-a) CO_2 will only develop when alveoli with very high V/Q ratios contribute to total ventilation. In other words, $PaCO_2$ will only increase when ventilation in proportion to VCO_2 can no longer compensate for inhomogeneity of intrapulmonary ventilation distribution.

FIGURE 2: THE PO_2/PCO_2 DIAGRAM FOR SINGLE GAS EXCHANGE UNIT AT FIO_2=0.21 AND ACO_2/O_2 EXCHANGE RATIO



DEAD SPACE:

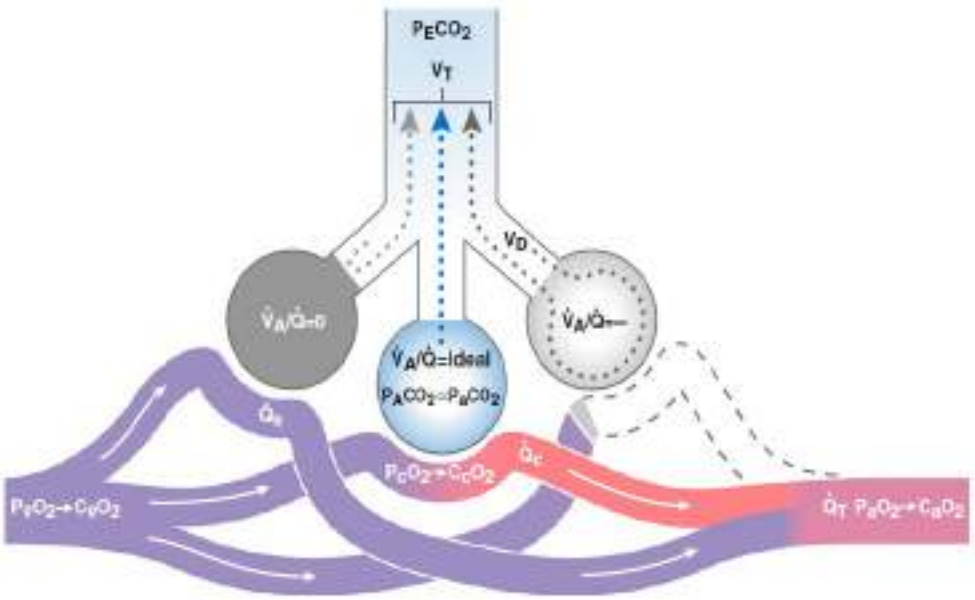
A single tidal breath, VT, and the expired volume per unit of time comprise a component that does not contribute to gas exchange, the dead space (V_d) as well as the volume of gas delivered to the alveolus (V_A).

$Vt = V_D + V_A$

Dead space ventilation consists of an anatomical (the conducting airways) and an alveolar component (ventilated but nonperfused alveoli and/or alveoli overventilated relative to perfusion). For a given V_A, metabolic VCO_2 determines $PaCO_2$, and any increase in V_D/V_T requests increases in V_E to maintain $PaCO_2$.

In summary, in patients with ARDS, impaired CO_2 clearance is mainly due to increased VD/VT (i.e., “wasted” ventilation) in ventilated but nonperfused lung regions. Hence, increasing V_E and/or decreasing V_D can allow maintaining $PaCO_2$; hypercapnia will occur when increasing V_E in proportion to metabolic VCO_2 can no longer compensate for inhomogeneous ventilation distribution.

FIGURE 3. RILEY’S 3 COMPARTMENT MODEL



VENOUS ADMIXTURE AND INTRAPULMONARY SHUNT

Pulmonary blood flow ("perfusion") guarantees that CO_2 and O_2 are transported from the tissues to the lung and vice versa. The pulmonary circulation is unique because:

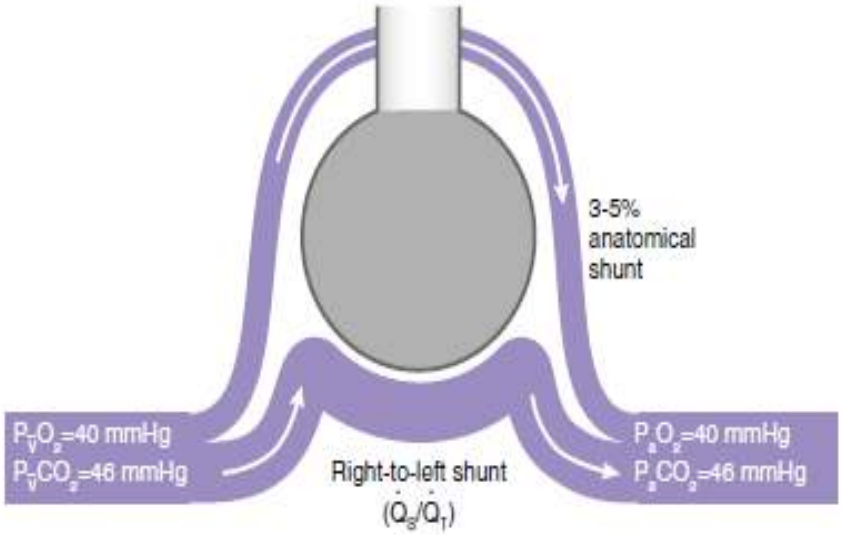
(1) Total cardiac output (QT) passes through one organ

(2) Due to the low pressures, flow distribution and, consequently, pulmonary vascular resistance depend on the surrounding alveolar pressures.

Pulmonary blood flow (Q_T) consists of flow through normally ventilated lung regions and a "shunted" component, the latter comprising the anatomical structures without contact with alveolar gas (Thebesian and bronchial veins), and an alveolar component originating from nonventilated (right-to-left shunt, Q_S) and/or hypoventilated alveoli. This alveolar component is called "physiological shunt" or "venous admixture" ($Q:V_A$).

According to the model by Riley and Cournand and in analogy to Vd/Vt, it can be referred to as "wasted" pulmonary blood flow.[10]

FIGURE 4. RIGHT TO LEFT ANATOMICAL SHUNT



Effect of Gravity

Gravitational force is a major determinant of the distribution of ventilation and perfusion: in the upright position, there is a near-linear increase of blood flow from the lung apex to the base due to gravitational force. Alveolar ventilation also follows this pattern, the slope being much flatter.

Because this gravitation-dependent variation of pulmonary blood flow is more pronounced than that of alveolar ventilation, V_A/Q ratios decrease from the apex to base of the lung, or, in the supine position, from ventral to dorsal lung regions. Several mechanisms have been identified to explain the beneficial effect of prone position on oxygenation. First, the prone position reduces the pleural pressure gradient and homogenizes transpulmonary pressure across the lung.[11,12]

Several factors can explain this effect of the prone position, including the reversal of gravitational lung weight gradients,[13] elimination of the compressive force of the heart on dorsal lung regions[14], and the release of the compression of abdominal contents on caudal regions of the dorsal lung.[15] The net effect is a homogenization of regional lung inflation, which increases in dorsal lung regions and decreases in ventral regions.

In addition, both animal and human studies showed that the distribution of pulmonary blood flow, which is prevalent in the dorsal lung in the supine position, surprisingly does not change when turning the patient prone.[16,17] Thus, the improvement in oxygenation in the prone position is due to a reduction in Q_S/Q_T resulting from the concomitant increase in the aeration in the dorsal lung regions, with dorsal recruitment being greater than ventral derecruitment, and the persistence of better lung perfusion in these regions.

PULMONARY VASCULAR TONE

Pulmonary vascular tone may cause marked regional V_A/Q differences, in particular as a result of hypoxic pulmonary vasoconstriction: local alveolar hypoxia induces regional vasoconstriction and thus reduces perfusion to hypo- and/or nonventilated lung areas, thereby improving gas exchange.

In patients with ARDS, increasing pulmonary vascular tone improved gas exchange[18,19], whereas reducing pulmonary artery pressure by hyperoxia and/or intravenous vasodilators further aggravated hypoxemia.

NONPULMONARY FACTORS

In addition to the degree of low V/Q and Q_S/Q_T, nonpulmonary factors affect gas exchange, namely FiO_2, cardiac output (Q_T) and VO_2. Q_T affects gas exchange both indirectly by its effect on O_2 extraction, and thus on PvO_2, and directly by modifying V_A/Q distributions. The complexity is that these factors may have various effects potentially influencing oxygenation in opposite directions.

EXTRAPULMONARY SHUNT

Intracardiac shunt via a patent foramen ovale (PFO) may also contribute to compromised gas exchange in ARDS. Under normal conditions, a PFO does not affect gas exchange, because the gradient between left and right atrial pressure precludes significant blood transfer from the venous to the arterial side. However, pulmonary artery hypertension is a common phenomenon in patients with ARDS and can lead to acute cor pulmonale.[20–22]

Prevalence of a PFO during ARDS has been reported in between 15 and 19% of patients and is often associated with acute cor pulmonale.[23] Frequently, in the presence of a moderate to large PFO shunting, there is a poor oxygenation response to PEEP. High PEEP may further increase the right atrial pressure, thereby increasing the occurrence and severity of right-to-left shunting due to PFO.[23,24]

Lowering PEEP and/or inhaled NO may reduce pulmonary hypertension, thus decreasing or abolishing right-sided shunting in some patients (14%), thereby improving oxygenation.[24]

RESPIRATORY MECHANICS IN ACUTE RESPIRATORY DISTRESS SYNDROME:

Three main physiological abnormalities characterize ARDS: hypoxemia; reduced capacity to eliminate CO_2; and reduced lung volumes and compliance. Whether all forms of ARDS share a common pathophysiologic course characterized by diffuse alveolar damage and neutrophil recruitment to the lungs is unclear,[25,26] but alterations of lung mechanics are ubiquitous and expose the remaining aerated lung to excessive ventilation. The subsequent local release of toxic mediators damages the capillary endothelium and alveolar epithelium. Once a patient with ARDS is placed under mechanical ventilation (MV), the most common abnormality is one of increased elastance secondary to this small lung size.

VENTILATOR-INDUCED LUNG INJURY:

MV, although often lifesaving in ARDS, may aggravate or initiate lung injury through several mechanisms, collectively termed ventilator-induced lung injury (VILI). VILI occurring at high lung volume is due to regional alveolar overdistension (so-called “volutrauma”), associated with high end-inspiratory transpulmonary pressure (PL), but not with high airway pressure (Paw) per se. VILI at low lung volume is due to high local tissue stress and parenchymal shear injury, supposedly caused by repetitive opening and closing of alveoli and distal small airways (“atelectrauma”), occurring when PL suddenly increases at early inspiration.[27]

VILI is associated with increases in pulmonary and systemic inflammatory mediators that may precipitate multiple organ dysfunction syndrome—a process that has been termed “biotrauma”[28]

RESPIRATORY MECHANICS DURING PASSIVE VENTILATION:

STATIC MEASUREMENTS FOR THE RESPIRATORY SYSTEM:

The equation of motion for the respiratory system, first proposed by Rohrer and based on Newton's third law[28], constitutes the fundamental theory of respiratory mechanics. It characterizes mechanical forces and provides the mathematical foundation for static measurements in clinical practice. During MV, both the ventilator and respiratory muscles can apply pressure to the respiratory system. The sum of applied pressures is equal to the sum of opposing pressures, namely, elastic recoil pressure (Pel), flow-resistive pressure (Pres), and inertial pressure (Pin) as follows:

Pvent + Pmus = Pel + Pres + Pin

Pvent is ventilator pressure; Pmus is muscle pressure

Paw + Pmus = ErsxΔV + RrsxV̇ + Irs·V̈,

where Ers represents respiratory system elastance (the inverse of compliance), ∆V is the volume difference from the resting volume, Rrs represents respiratory system resistance, and Irs represents inertance. **V̇** is the rate of change in volume and **V̈** is the rate of change in flow. Other than in situations such as high-frequency ventilation or coughing, inertance is negligible.

During passive ventilation, the respiratory muscles are relaxed and the Pmus is nil. ∆V is the sum of inspired volume (Vinsp) above end-expiratory lung volume (EELV) and EELV above FRC. The product of Ers and EELV above FRC is equivalent to the total Pel at the end of expiration (total positive end-expiratory pressure [PEEPtot], namely, the sum of PEEP and intrinsic PEEP).

Paw=Ers x Vinsp+ Rrs x V̇. + PEEPtot

STATIC MEASUREMENTS FOR PARTITIONING LUNGS AND CHEST WALL

The measurement of Paw allows the description of the total respiratory system. To differentiate the mechanical properties of the lungs from those of the chest wall requires measuring the pleural pressure (Ppl). The pressure applied on the lungs is the difference between Paw and Ppl is called the Pl. When the respiratory muscles are relaxed, the pressure applied on the chest wall (Pcw) is the difference between Ppl and body surface pressure (Pbs); the pressure applied on the total respiratory system (Prs) is the difference between Paw and Pbs.
Hence,

Prs = Paw − Pbs = (Paw − Ppl) + (Ppl − Pbs) = PL + Pcw

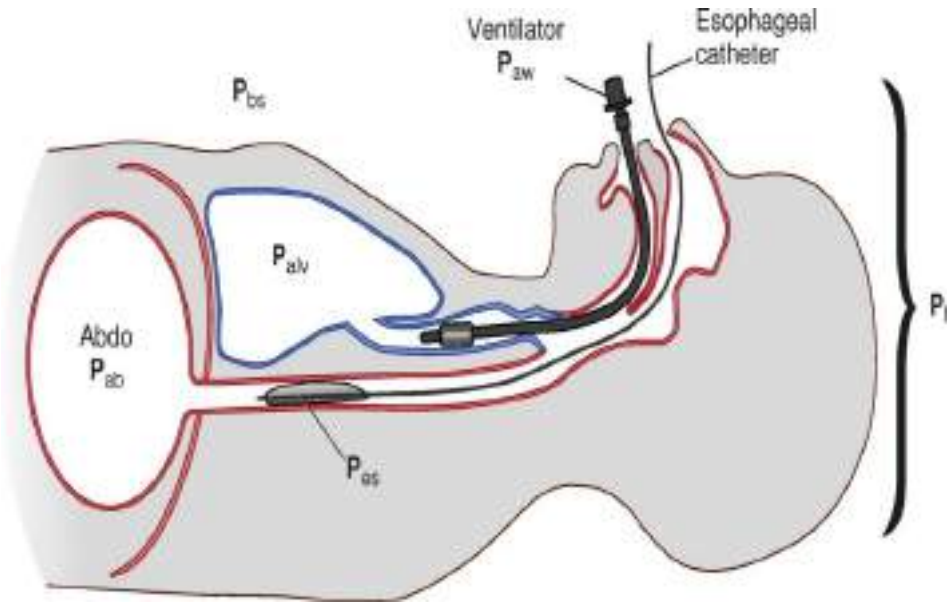
Pbs is usually atmospheric pressure, which, by convention, is referred to as zero. All of the mechanical properties of the respiratory system can be partitioned into lungs and chest wall by separating pressures.

The change in the elastic pressure of the respiratory system is the sum of the change in lung elastic pressure and the change in chest wall elastic pressure

Ers= EL + Ecw

where El and Ecw denote lung and chest wall elastance (the inverse of lung and chest wall compliance). Estimating Ppl with an esophageal balloon catheter has made all these calculations possible.[29,30] As the esophageal pressure (Pes) obtained through a catheter approximates Ppl, Equations can be restated by replacing Ppl with Pes. Pl is calculated as the difference between Paw and Pes, and it reflects the distending pressure of the lung.

FIGURE 5. ILLUSTRATION OF MEASUREMENTS



Artwork by Vicky Earle

The clinician can directly measure the pressure from the ventilator at the airway opening (airway pressure [Paw]) and reference it to body surface pressure (Pbs). Esophageal pressure (Pes) may also be directly measured with a balloon manometer. Transpulmonary pressure (Pl) = Paw − Pes. The alveolar pressure (Palv) can be measured from Paw during end-inspiratory (plateau) and end-expiratory (total positive end-expiratory pressure) holds. Abdominal pressure (Pab) can be measured in the stomach or the bladder.

One important limitation is that the Ppl is not uniform, and a pressure gradient between non-dependent and dependent parts of the pleural space is enlarged in ARDS. Therefore, even if the Pes accurately measures an intrathoracic pressure, it only reflects the distending pressure at one level of the lung, adjacent to the position of the esophagus.

Clinical Reference Ranges of Respiratory Mechanics

Interpreting the measured variables of respiratory mechanics requires an understanding of their physiological meanings as well as reference ranges and/or safe limits. However, the description of respiratory mechanics (particularly for lung and chest wall properties) in large cohorts is lacking.

TABLE 3. CLINICAL REFERENCES FOR CALCULATION OF RESPIRATORY MECHANICS

Clinical References for Calculation of Respiratory Mechanics			
Derived Calculations	**Average Value in ARDS**[31]	**Estimated Normal Values**[32]	**Explanation of Reference Range**
Compliance of respiratory system, ml/cm H2O	38	1.6% of VC ml/cm H_2O	An average VC in normal subjects is around 4,000 ml; the predicted Crs would be 1.6% × 4,000 = 64 ml/cm H2O
Compliance of lungs, ml/cm H_2O	55	2.9% of VC ml/cm H_2O	Roughly predicted range: 90–140 ml/cm H2O
Chest wall compliance, ml/cm H_2O	125	3.6% of VC ml/cm H2O	Roughly predicted range: 100–200 ml/cm H2O
Elastance of respiratory system(Ers), cm H_2O/L	26	0.62 cm H2O/1% VC (L)	An average VC in normal subjects is 4 L; this gives a predicted Ers

			as 0.62 ÷ 4% = 16 cm H2O
Elastance of lungs (El), cm H_2O/L	18	0.34 cm H_2O/1% VC (L)	An average predicted value would be around 9 cm H2O/L
Elastance of chest wall (Ecw), cm H_2O/L	8	0.28 cm H_2O/1% VC (L)	An average predicted value would be around 7 cm H2O/L
E_L/Ers	0.70	0.55	Estimated from predicted values of El and Ers
Resistance of respiratory system (Rrs), cm H_2O/L/s	-	8–12 at 60 L/min of square-wave inspiratory flow	This reference value is valid for inspiration only and depends on flow rate and the size of the endotracheal tube

CURRENT THERAPIES:

Despite considerable advances in our knowledge regarding the pathophysiology of ARDS, few insights into the biological mechanisms of lung injury and repair, advances in supportive care including extracorporeal membrane oxygenation, there remains no effective direct therapy for ARDS.

Numerous clinical studies have been conducted on patients with ARDS, but great advances in the care of the patients are still lacking and supportive therapies remain the mainstay in ARDS management.

PROTECTIVE MECHANICAL VENTILATION:

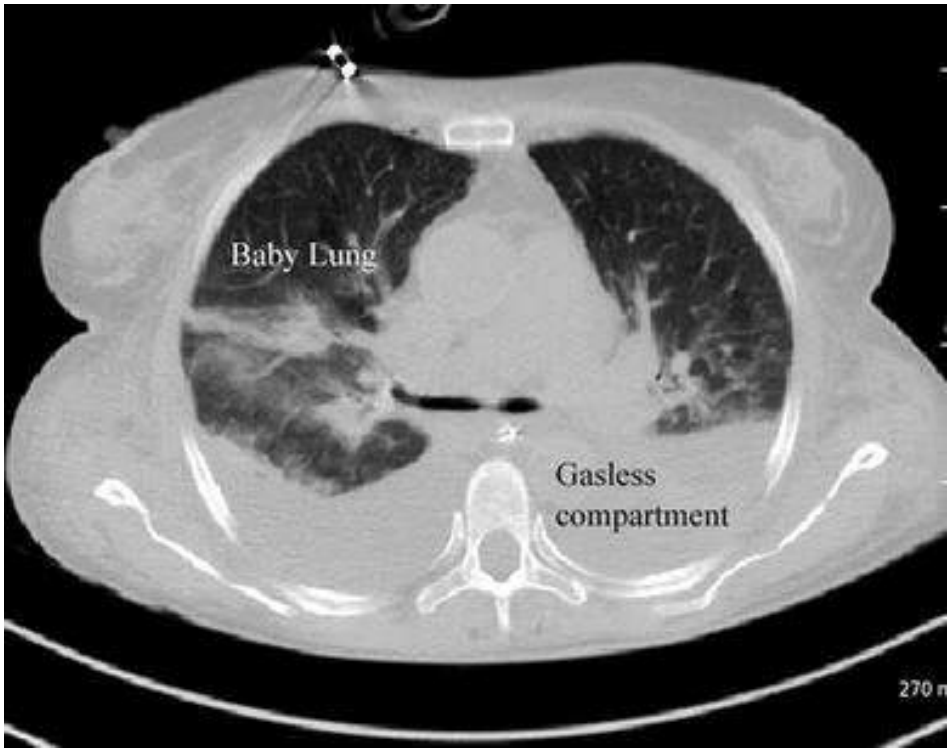
There is a large body of evidence from interventional and clinical studies demonstrating that mechanical ventilation, particularly in the setting of lung injury, can exacerbate functional and structural alterations in the lung.[33] It is noteworthy that mechanical ventilation not only perpetuates lung injury but also contributes to both the morbidity and mortality of ARDS.[26]

The Baby Lung Concept:[34]

ARDS was initially conceived of as diffuse homogenous increases in elastance throughout the lung parenchyma. Computed tomography (CT) studies demonstrated that abnormalities in ARDS are mostly regional, with areas of dense consolidation or atelectasis and other areas with normal, or near-normal, aeration. This loss of aerated lung is reflected in reduced FRC, which may be as low as 20–30% of theoretical values expected for healthy subjects.[35]

Gattinoni and colleagues[36], using quantitative CT scan analysis, found that the reduction in global compliance was mostly explained by the loss in aerated volume. Key insights derived from these observations were that the aerated lung in ARDS has nearly normal regional mechanics and that the ventilated lungs are not stiff, but small. This suggests that the “normal” lung areas are subject to increased inflammation, potentially in part because they are overventilated to compensate for the great loss of alveolar units.

FIGURE 6. BABY LUNG CONCEPT



A representative CT scan image of an ARDS patient showing that the ARDS lung can be modelled in one nearly normal region (having dimensions similar to those of a healthy baby) and a gasless region)

USE OF RESPIRATORY MECHANICS TO GUIDE VENTILATION IN ARDS:

VT, Pplat:

The concept that the limitation of end-inspiratory lung stretch may reduce mortality in ARDS patients, culminated in the NIH-sponsored multicenter study of patients with ARDS. In this trial, patients randomized to receive a lower tidal volume (Vt) [4-6 mL/kg predicted body weight (PBW), and maintenance of plateau pressure between 25 and 30 cm of H_2O] had a survival benefit. Mortality was reduced from 40% in the conventional arm to 31% in the low Vt arm (CI, 2.4-15.3% difference between groups).[6]

The benefit in terms of mortality and ventilation free days did not appear to be related to the value of the lung compliance at baseline or the underlying risk factor for ARDS.[6] Of note, the survival benefit was associated with a reduction of plasma IL-6 concentration, supporting the hypothesis that a lung-protective strategy limits the spill over into the systemic circulation of inflammatory mediators, which in turn may induce multiple system organ failures.[26]

In addition to lung over-distention, cyclic opening and closing of small airways and alveolar units (so-called atelectrauma) can also lead to lung injury.[37] Several clinical trials have been conducted in ARDS patients to examine the effects of an “open lung” approach in which the application of recruitment manoeuvres and higher levels of PEEP may limit atelectrauma.

In 2008 a French multi-centre randomized control trial (EXPRESS study) addressed the superiority of an open lung approach in which PEEP was titrated to the highest value possible keeping Plateau pressure <28-30 cm Of H_2O.[38] In the control arm, PEEP was set between 5 and 9 cmH2O. In both groups, Vt was <6 mL/kg PBW. Patients treated according to the open lung approach had significantly more ventilator-free days and organ failure-free days; however, hospital, 28-day and 60-day mortality were not different between the study groups, patients. Of note, patients who now would be considered to have moderate to severe lung injury (P/F <200) tended to have lower 28-day mortality in the higher PEEP group compared to patients treated with lower PEEP.

Pplat is the sum of PEEP or PEEPtot and ΔP. The incidence of complications, such as pneumothoraces, has markedly decreased since the use of lower Pplat. [36]

In two randomized studies, Amato et al, and Villar et al. and colleagues examined the effect of a composite strategy that minimized tidal

volume, adopted lung recruitment manoeuvres, and applied a level of PEEP above the closing pressure of the lung. Although the intervention arms decreased mortality, the studies were criticized due to relatively small sample sizes and relatively high mortality in the control arms. The ARDS Network performed a second large clinical trial comparing lower vs. higher levels of PEEP (the ALVEOLI study).[39] The trial was stopped early for futility, showing a trend to worse outcome in the higher PEEP arm, although there was an imbalance in patient characteristics at baseline favouring the control arm; the mean age of the higher PEEP arm was higher (54±17 vs. 49±17, $P<0.05$), the mean PaO_2/FiO_2 was lower (151±67 vs. 165±77, $P<0.05$), and there was a trend to higher APACHE III scores, at baseline.

Similar results were obtained in the Canadian Lung Open Ventilation (LOV) clinical trial.[40] The PEEP values were slightly higher compared to those of the previous ALVEOLI study. The study enrolled 985 patients and it failed to demonstrate any difference in mortality in the two groups (36.4% and 40.4% in the treatment and control groups respectively). The use of rescue therapies and death from refractory hypoxemia were less in the LOV - higher PEEP group.

A recent meta-analysis that incorporated trials (from 1996 to January 2010) comparing higher vs. lower levels of PEEP concluded that there is no difference in mortality applying lower vs. higher levels of PEEP in patients with mild ARDS. However, in the subgroup of patients with severe ARDS, as defined by a PaO_2/FiO_2 <200, there was a benefit from higher levels of PEEP.[41]

Driving pressure (ΔP):

Amato and colleagues proposed that lung injury may be due to swings in pressure during ventilation rather than an absolute maximum level of Pplat.[42] This value they have termed as Driving pressure (ΔP), corresponds to the elastic pressure swing, ΔPel, rs = ΔV × Ers. ∆P thus describes the relationship between Vt and the lung volume available to receive the breath. ∆P equals Vt/Crs, and Crs is proportional to

FRC.[43]They used a statistical tool known as multilevel mediation analysis to analyse individual data from 3,562 patients with ARDS that were enrolled in nine randomized trials, it was demonstrated that ΔP was the pulmonary mechanical variable most predictive of 60-day survival in ARDS.[44] Limiting ΔP—possibly keeping it below 14 cm H2O can be achieved either by decreasing Vt or increasing Crs.[44,45] Vt reduction may require volumes that do not support adequate oxygenation or sufficient CO_2 elimination. Increasing Crs by altering PEEP may not always be achievable.

Stress and strain:

Lungs of patients with the same bodyweight ventilated with the same Vt may be subjected to different forces dependent on the size of the functional lung. This is expressed by the mechanical concepts of stress and strain.

Stress is the net force acting on a material structure, for instance, a lung strip connecting the hilum to visceral pleura, causing deformation (i.e., strain), divided by the cross-sectional area of this strip. In respiratory mechanics, lung stress reflects the net distending pressures applied on the lung parenchyma, opposed by the elastic pressures generated by the tensioned alveolar walls and lung scaffold. Stress is equal to Pl (Paw − Ppl) under zero flow conditions. Strain represents the deformation experienced by a structure, and is defined as the change in length (Δl) or volume compared with the structure's initial length (l_0) or volume, assumed to be the natural, unstressed condition.

Strain = VT/FRC[46]

The generation of strain above specific levels is associated with clinical and biochemical markers of lung injury.

Pl and Strain:

It may be possible to estimate strain from measurements of stress, as the two values are linked by the specific elastance of the lung (Elspec) such that:

strain=stress/ELspec[46]

Thus, if the net distending pressure, Pl, is known, strain may be estimated:

strain=PL/ELspec

The value of Elspec is approximately 13 cm H2O, a value that varies moderately during disease in the range of tidal ventilation.[46] Thus, by measuring transpulmonary stress, strain may be inferred (i.e., ~1/13 of transpulmonary stress).

Transpulmonary Pressure guided ventilation:

Transpulmonary pressure (Pl) has traditionally been used to describe the pressure difference (or pressure drop) across the whole lung, including the airways and lung tissue and hence Transpulmonary pressure is defined as the pressure difference between the airway opening and the pleural surface.

The transpulmonary pressure can be partitioned into the pressure drop down the airway (Pao − Palv), where Palv is alveolar pressure, and the pressure drop across the lung tissue, known as the elastic recoil pressure of the lung [Pel(L) = Palv − Ppl].

Alternate Definitions of Transpulmonary Pressure:

Transpulmonary Pressure Has Been Redefined as the Pressure across Lung Tissue, (Palv − Ppl). Numerous relatively recent texts and articles have used the term “transpulmonary pressure” or “Pl” to describe Palv − Ppl, that is, Pel(L), the elastic recoil pressure of the lung tissue (i.e., without considering the pressure drop down the airway). Among

these are John West's Respiratory Physiology, the Essentials, Weinberger's Principles of Pulmonary Medicine, Schwartzstein's Respiratory Physiology, a Clinical Approach, and other current reviews and journal articles.[47,48]

Thus, **Pl = (Pao − Palv) + (Palv − Ppl)**

In subjects breathing without equipment, Pao is the pressure at the mouth or nose, whereas, in patients who are intubated, Pao is the pressure in the external port of the endotracheal tube or ventilator tubing, which is often called airway pressure (Paw). All pressures are measured relative to atmospheric pressure (0 cm H_2O).

Although Pao is easily measured continuously, Ppl is not practical to measure directly. However, Ppl can be estimated by measuring esophageal pressure (Pes), allowing Pl to be continuously estimated as Pao − Pes.

The elastic recoil pressure of the lung, Pel(L) = Palv − Ppl, is the relevant pressure when considering the stress applied to the lung tissue. Determination of Pel(L) requires estimation of Palv, which is not easily measured directly. Fortunately, under static conditions when the intrapulmonary airways are open and there is no airflow or temporal acceleration of gas, Pao − Palv = 0, and therefore Pao = Palv and Pl = Pel(L), a reasonable assumption in the absence of gas trapping.

Pl Is Continuously Measurable; Pel(L) Is Not

Pl and Pel(L) both vary continuously in time. However, Pel(L) cannot be measured continuously, because it requires determination of Palv, which can only be measured when there is no pressure drop down the airway.

Although continuous estimation of transpulmonary pressure is feasible, it is usually assessed at two critical points during the breathing cycle:

the end of inspiration, relevant to prevent hyperinflation, and the end of expiration, relevant to avoid lung derecruitment.[49]

In the clinical ground, the conventional estimate of Ppl requires the measurement of Pes with a balloon-tipped catheter. Briefly, Pes is considered to be representative of the average value of Ppl surrounding the lungs, although this assumption is largely based upon studies in healthy subjects in the upright position.[50] This assumption is based on the anatomical proximity of the lower third of the esophagus to the pleural space and the transmission of Ppl through its wall, as it mainly acts as a passive membrane. Only in recent years, evidence for its effectiveness is beginning to be found. several authors raised concerns about the accuracy of Pes measurements in supine patients with altered lung function.

TABLE 4. LIMITATIONS OF Pes MEASUREMENT

1. Elastic recoil of the balloon (if overinflated)
2. Elastic recoil of esophageal wall
3. The vertical hydrostatic gradient of lung inflation
4. Pressure transmitted by the mediastinum
5. Elastic recoil of the diaphragm
6. Transmission of intra-abdominal pressure
7. Presence of inter-regional differences in pleural pressure
8. Asymmetric lung disease
9. Presence of pleural effusion

Elastance-derived measurement:

In an attempt to remove the confounding influence of the mediastinal weight, assuming that its influence is constant throughout the respiratory cycle, this method, proposed by Gattinoni et al.[51], estimates the end-inspiratory Pl as the product of plateau pressure times the ratio between lung (El) and respiratory system elastance (Ers). Similarly, end-inspiratory Ppl is plateau pressure times the ratio between Ecw and Ers. In other words, this method estimates the

portion of Paw that is spent to inflate the lungs only, and the portion that is required to move the chest wall, based on the relative contribution of El and Ecw to Ers.

The assumption underlying this method is that, for mathematical reasons, Pl and Ppl are 0 at atmospheric pressure: if true pressures are higher or lower than 0 when Paw is 0, the calculated pressures will be under or over-estimated, respectively. Secondly, since elastance is calculated using the tidal change in Paw and Ppl, these variations should be linear during tidal inflation.

With this method, given that in a system composed of two elastic structures in series:

Paw = Pl + Ppl and Ers = El + Ecw;
Then
Pl = Paw × El/Ers and Ppl = Paw × Ecw/Ers.

In a study conducted by Bastia et al where they subjected invasively ventilated pigs to unilateral lung injury via surfactant lavage and high tidal stretch which was instituted with temporary bronchial blockade occluding the contralateral lung they found that vertical pleural pressure gradients existed but no significant pleural pressure gradients were present between the left and right hemithorax.[52]

These findings are expected given that lung injury induced via the airway should not alter chest wall mechanical properties. Normally, mechanical coupling of the left and right hemithoracic pleural spaces occurs via:
1) Mechanical coupling of the left and right rib cages with symmetrical movement during respirations and
2) Compliance of mediastinal structures separating the hemithoraces. In contrast to unilateral lung injury, decreased mediastinal compliance can create asymmetric hemithoracic chest wall mechanics, as may

occur with mediastinal fibrosis resulting from thoracic surgery or chest radiation therapy.

In their swine model, esophageal pressure corresponded closely with posterior pleural pressure. However, in humans, esophageal pressure approximates the midthoracic pleural pressure, a contrast explained by differences in swine versus human chest wall shape and anatomic position of the esophagus in the thorax.[53]

In a study conducted by Takeshi et al on pig and human cadavers, they found that Pes values were accurate if calibrated properly.[53] They also found that Pl calculated from Pes (either inspiratory or expiratory) accurately reflected Pl in the lung regions adjacent to the esophageal balloon (i.e., dependent to middle lung), if correctly calibrated.

On the other hand, end-inspiratory Pl, as obtained with the elastance-derived method, was found to reflect the “true” local Pl in the non-dependent areas.

There is, however, no unique value of Ppl, and a gradient of pressure exists between the upper, anterior part of the pleural space when the patient is lying supine, also referred to as the ‘non-dependent’ pleural regions, vs. the dorsal, posterior part of the pleural space, also referred to as the ‘dependent’ pleural regions. This gradient explains the distribution of densities in the lung and may reach values around 10 cm of H_2O. Thus, Pes at end-expiration is potentially useful to guide PEEP settings to counter atelectasis in dependent to middle lung regions.

How transpulmonary pressure could guide PEEP?

Since Paw and tidal volume have proven inadequate surrogates for lung stress and strain,[54] the use of Pl has been proposed as a better means of adjusting the settings of mechanical ventilation.

Positive end-expiratory pressure (PEEP) theoretically maintains positive lung distending transpulmonary pressure at end-expiration, i.e.

PEEP minus Ppl, leading to minimizing dependent collapse. However, Ppl is variable and unpredictable without specific monitoring as a result of abnormal chest wall mechanics and/or increased oedema, so it is uncertain if PEEP can maintain positive PL without knowing Ppl.

Oesophageal manometry is a non-invasive technique to measure Ppl and thus estimate the lung distending transpulmonary pressure. One could envision that an ideal PEEP titration strategy in acute lung injury might begin by targeting Pl near 0 cm H_2O at end-expiration to attenuate atelectrauma. Some measure of inspiratory stress or strain (e.g., airway or transpulmonary driving pressure, end-inspiratory Pl, or electrical impedance tomography–derived strain)[55] might then be used to determine whether protective ventilation can be attained at a Vt of 6 ml/kg predicted body weight without significant hyperinflation. If hyperinflation persists, Vt would be lowered until hyperinflation abates. If gas exchange impairment precludes further reduction in Vt despite increasing respiratory rate, then either

1) PEEP would be lowered, and negative end-expiratory Pl would be tolerated in recognition of the greater contribution of hyperinflation to clinically significant lung injury or

2) if deemed appropriate, an extracorporeal gas exchange could be considered to enable further reduction in Vt when appropriate.

FIGURE 7: THEORETICAL RELATIONSHIP OF PL WITH THE COMPETING RISKS OF VENTILATION-INDUCED LUNG INJURY (VILI) FROM OVERDISTENSION AND ATELECTRAUMA

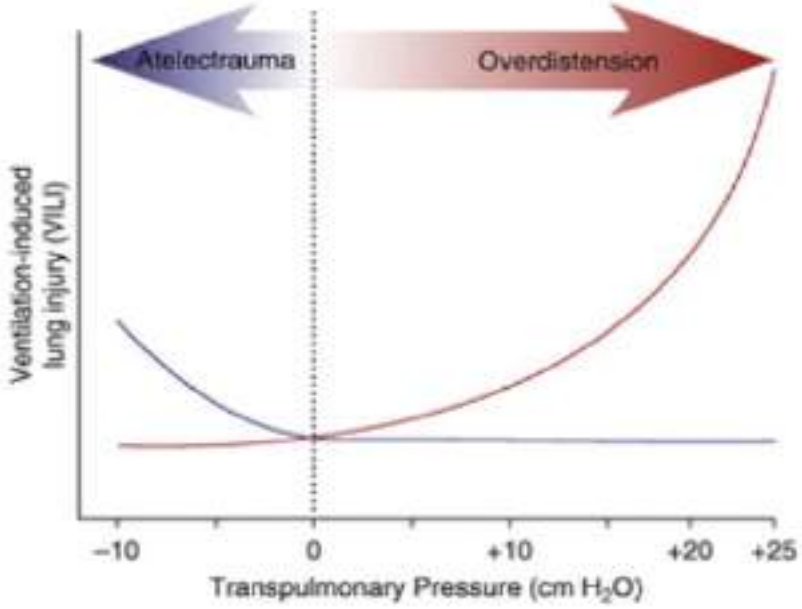
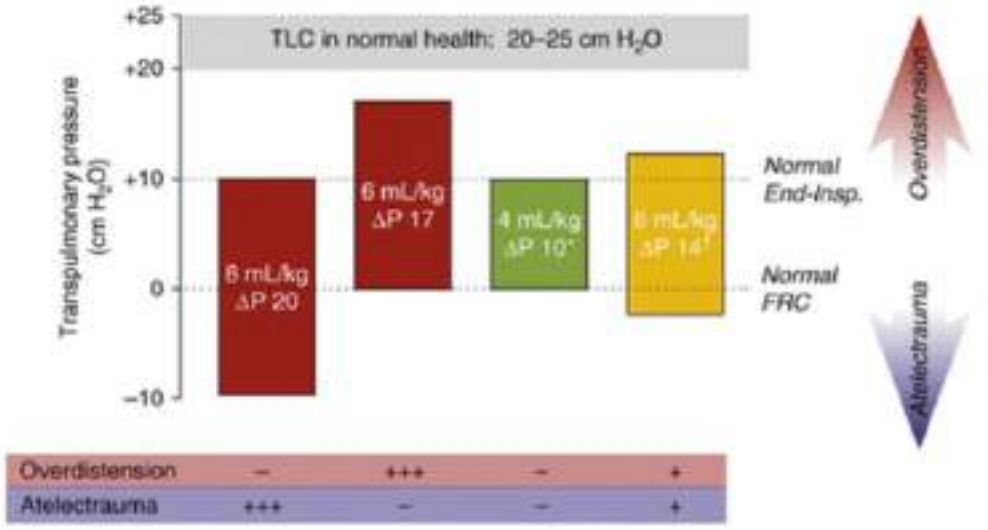


FIGURE 8: VENTILATOR TITRATION STRATEGY WITH RISK OF VILI



Maximal lung protection may occur when positive end-expiratory pressure is set to achieve an end-expiratory Pl near 0 cm H_2O and Vt is targeted to a driving Pl of ≤10–12 cm H_2O. Boxes reflect the range of Pl during tidal ventilation in a theoretical patient with severe acute respiratory distress syndrome. Red, yellow, and green colored boxes denote high, moderate, and low risk of VILI, respectively.

For reference, in the lean, healthy, spontaneously breathing adult, Pl is ~0 cm H_2O at FRC, 10 cm H_2O at end-inspiration during normal tidal breathing, and 20–25 cm H_2O at TLC.

Such a PEEP strategy has not been tested in a clinical trial. In the EPVent-2 trial of moderate to severe acute respiratory distress syndrome,[56] esophageal pressure–guided PEEP was targeted to an end-expiratory P l between 0 cm H_2O and +6 cm H_2O depending on the FiO_2 requirement. Although speculative, it is conceivable that some patients in this protocol experienced overdistension that countered the protective effects against atelectrauma. The EPVent-2 protocol did prescribe limits to “peak stress,” prohibiting end-inspiratory Pl from exceeding 20 cm of H_2O.

In trials of mechanical ventilation involving patients with ARDS, in which V_T and PEEP were included as independent variables, the dependent quantity ΔP was the variable that was most strongly associated with survival. The main goal of mechanical ventilation is to achieve adequate oxygenation and ventilation while minimizing Ventilator-induced lung injury.

Although translation to demonstrable clinical benefit has proven elusive, preclinical studies continue to suggest a protective role for precise PEEP titration in severe acute lung injury. Competing effects of overdistension and atelectrauma with higher and lower PEEP, respectively, almost certainly have contributed to past unsuccessful trials.

MATERIALS AND METHODS

This prospective study was conducted in Dayanand medical college & hospital for duration of 1 year from April 2020 to April 2021 after obtaining approval from institutional ethics board.

SOURCE OF DATA:

GROUP ALLOCATION:

Patients were allocated to either of two groups based on computer-generated random numbers.

GROUP T received transpulmonary pressure guided ventilation.

GROUP C received conventional ventilation.

METHOD OF COLLECTION OF DATA

INCLUSION CRITERIA:

- Patients were included in the study if they had moderate-to-severe ARDS according to the Berlin criteria.
- Duration of ARDS 36 hours or less from meeting final Berlin criterion.
- Age more than 18 years.

EXCLUSION CRITERIA:

- Received mechanical ventilation for more than 96 h.
- Recently treated for bleeding varices, stricture, haematemesis, esophageal trauma, recent esophageal surgery or other contraindication for nasogastric tube placement.
- History of lung or liver transplantation.
- Evidence of active air leak from the lung (including bronchopleural fistula, pneumothorax, pneumomediastinum or air leak from existing chest tube).
- Severe chronic liver disease (Child-Pugh Score ≥12).
- Patients not committed to full support.
- Inability to get informed consent from the patient or surrogate.
- Use of rescue therapies before enrolment (including nitric oxide, ECMO, prone positioning)

OUTCOME:

Primary outcome:

- Improvement in PaO_2 /FiO_2 ratio, A-a gradient, a/A ratio.

Secondary outcome:

- Improvement in respiratory system compliance.
- VILI like spontaneous pneumothorax, pneumomediastinum.
- Improvements in CO_2 exchange.

Measurements and Experimental Protocol:

While undergoing treatment, the subjects were made supine, with the head of the bed elevated to 30 degrees. Airway pressure, tidal volumes and other respiratory parameters were recorded during mechanical ventilation.

Pes was measured via an air-filled balloon catheter inserted in the esophagus. For this study, we used a MBMed BA-A-008 esophageal balloon catheter.

FIGURE 9. ESOPHAGEAL BALLOON CATHETER

The catheter was inserted through the nostril or the mouth and was progressively pushed down to the stomach (usually at 50–60 cm,

depending on the patient's height), inflated, and was connected to a pressure transducer. The latter was linked to the pressure port of the ventilator. Placement of the balloon in the stomach was confirmed by a transient increase in pressure during a gentle compression of the abdomen and by a qualitative change in the pressure tracing (i.e., an increased cardiac artefact) as the balloon was withdrawn into the esophagus. Likewise, ventilator insufflation or the patient's inspiratory effort showed a positive swing on the tracing.

The catheter was then slowly withdrawn to reach the lower and middle third of the esophagus, at which point cardiac artefacts appeared on the waveform (distance from the teeth is usually 35–45 cm). The middle third of the esophagus was where the pressure measurement was more stable, uniform, and was less influenced by external structures.

In a passive patient (eg, comatose, deeply sedated, paralyzed or not), machine insufflation lead to positive deflection due to an increase in Pes (Fig. 7A); in an actively breathing patient, effort leads to a negative swing due to a decrease in Pes (Fig. 7B)

FIGURE 10A: WAVEFORMS IN PASSIVELY BREATHING PATIENT

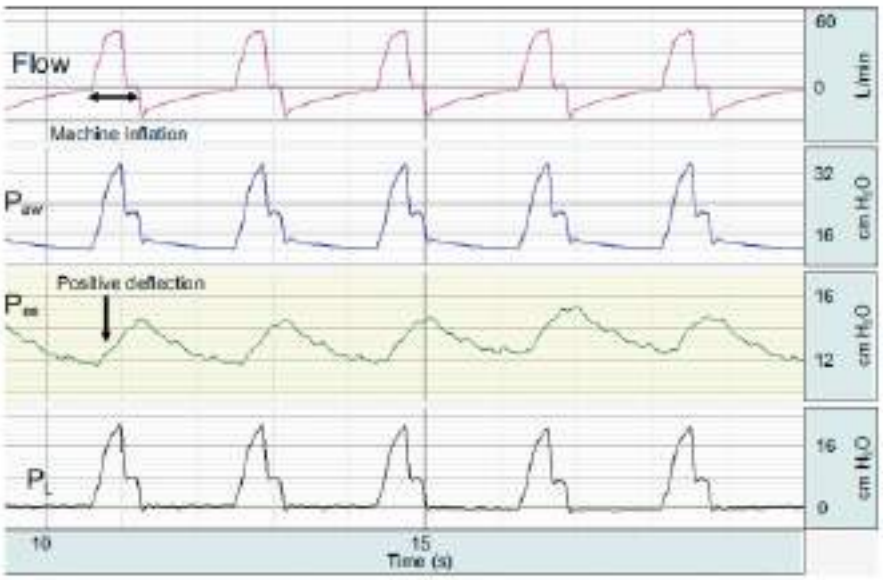
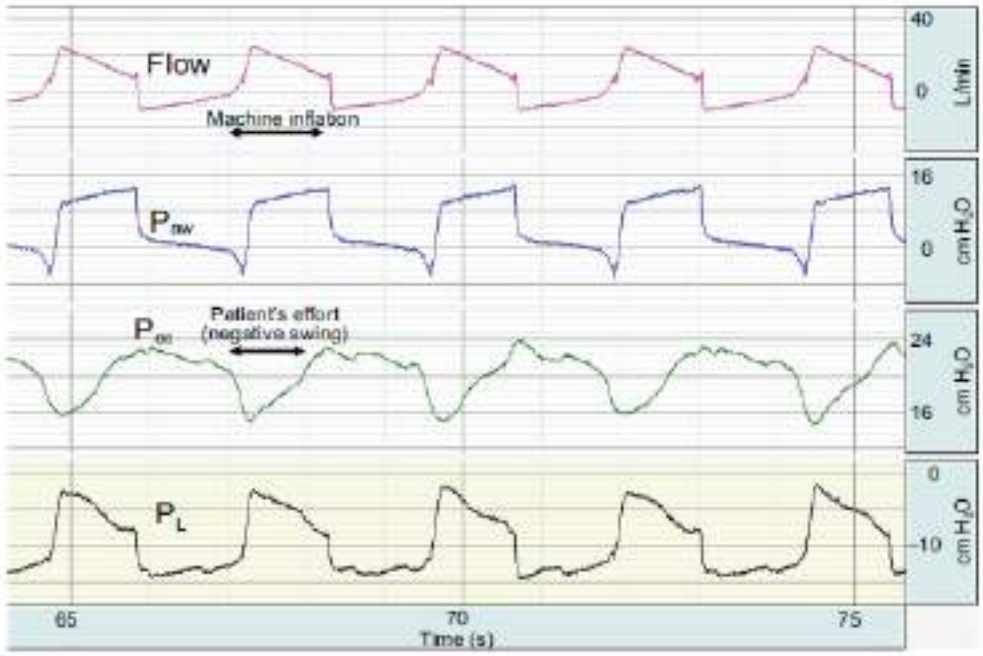


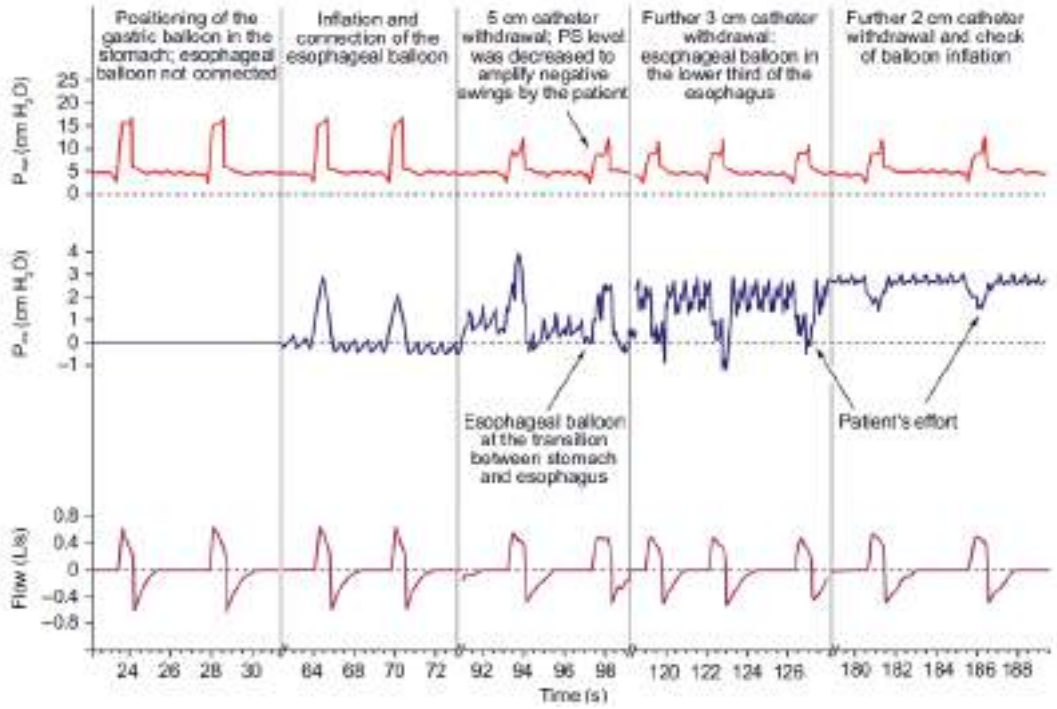
FIGURE 10B: WAVEFORMS IN SPONTANEOUSLY BREATHING PATIENT



VALIDATION OF THE MEASUREMENT:

To ascertain that the catheter was placed in the appropriate location and provided an acceptable proxy for Ppl an occlusion test was done.[57] The principle of this test was to occlude the patient's airway opening so that any change in pressure should be the same in the whole occluded system. In other words, when a patient made an inspiratory effort during the occlusion, there was no flow in the system and the change in Pes (ΔPes) was equal to the change in the airway opening pressure (ΔPaw). This means the ratio of ΔPaw to ΔPes should be close to 1. In practice, the Pes measurement was considered a reliable surrogate of Ppl when this ratio is between 0.8 and 1.2. By applying the same concept in passively ventilated patients with a lack of inspiratory efforts, a modified occlusion test has been proposed, consisting of an external manual pressure applied to the rib cage during an expiratory pause.

FIGURE 11. PRESSURE WAVEFORMS DURING INSERTION OF AN ESOPHAGEAL CATHETER


Positioning of the gastric balloon in the stomach; esophageal balloon not connected
Inflation and connection of the esophageal balloon
5 cm catheter withdrawal; PS level was decreased to amplify negative swings by the patient
Further 3 cm catheter withdrawal: esophageal balloon in the lower third of the esophagus
Further 2 cm catheter withdrawal and check of balloon inflation
Esophageal balloon at the transition between stomach and esophagus
Patient's effort
Time (s)

Paw = airway pressure; Pes = esophageal pressure; PS = pressure support.

ARTIFACTS AND TROUBLESHOOTING:

Even when the catheter is in the correct position and the balloon inflation is optimized, artefacts such as the transmission of the heartbeat can impede Pes-based estimation of pleural pressure, particularly when the cardiac oscillations are of the same magnitude as the Pes swings. Changing the angle of the bed to have the patient in more of a seated position or withdrawing the catheter a few centimetres can, in some cases, decrease cardiac artefacts.

After these initial measurements, patients were randomly assigned with the use of a block-randomization scheme to the control or esophageal pressure-guided group. Each patient, while under heavy sedation or paralysis with an R.A.S.S. score of 0 to -1, underwent a recruitment manoeuvre to standardize the history of lung volume. The patients in the esophageal-pressure-guided group underwent mechanical

ventilation with settings determined by the initial esophageal-pressure measurements. Tidal volume was set at 6 ml per kilogram of predicted body weight. PEEP levels were set to achieve a transpulmonary pressure of 0 to 12 cm of water at end-expiration, according to a scale based on the partial pressure of arterial oxygen (PaO_2) and the fraction of inspired oxygen. For FiO_2 between 0.5 to 1 PTP (end-expiratory hold) of 8 to 10 cm was used and for FiO_2 less than 0.5 PTP (end-expiratory hold) of 4 to 8 cm was used. We also limited tidal volume to keep transpulmonary pressure at less than 25 cm of water at end inspiration.

Patients in the control group were treated according to the low-tidal-volume strategy reported by the ARDS Net study of the National Heart, Lung, and Blood Institute.[6] These patients were ventilated using volume control mode with the tidal volume set at 6 ml per kilogram of predicted body weight and PEEP is based on the patient's PaO_2 and FiO_2.

In both groups, the goals of mechanical ventilation were a PaO_2 of 55 to 120 mm. of Hg or a pulse-oximeter reading of 88 to 98%, an arterial pH of 7.30 to 7.45, and a partial pressure of arterial carbon dioxide ($PaCO_2$) of 40 to 60 mm Hg.To reduce the need for frequent manipulation of the ventilator settings, the goals for oxygenation in both groups were relaxed from the narrow range of PaO_2 values in the ARDS Net study (55 to 80 mm Hg) to a broader range of 55 to 120 mm Hg. All measurements were repeated 5 minutes after the initiation of interventional or control ventilation and again at 6 and 12 hours.

The primary end point of the study was the comparison of arterial oxygenation, as measured by the ratio of PaO_2 to FiO_2 (PaO_2:FiO_2) at 6 hours and 12 hours after ventilation using either strategies and A-a gradient and a/A ratios at 0 and 12 hours. The secondary end points included respiratory system compliance and CO_2 gas exchange. VILI was followed up to 7 days.

STATISTICAL ANALYSIS:

SAMPLE SIZE ESTIMATION:

In evaluating the PaO_2:FIO_2 at 6 hours, we decided a priori that a clinically important change in the PaO_2:FIO_2 would be approximately 20%, with measurement error taken into account. To determine sample size, we chose a minimal average between-groups difference of 40 in the PaO_2:FIO_2. We conservatively estimated the standard deviation to be 100 (equivalent to a coefficient of variation of 250%); based on this estimate, a sample of 50 patients per group would be required to detect a difference of 40 in the PaO_2:FIO_2 with 80% power and a two-tailed alpha value of 0.05.

Continuous variables with normal distribution are presented as means (±SD) and compared with the use of the Student's t-test. Continuous variables with non-normal distributions are presented as medians and interquartile ranges and compared with the use of the Mann–Whitney test. Dichotomous or nominal categorical variables are compared with the use of the chi-square test with normal approximation or Fisher's exact test, as appropriate. A two-tailed P value less than 0.05 was considered to indicate statistical significance. Statistical analysis was performed using SPSS version 17.

OBSERVATIONS AND RESULTS

We enrolled 100 patients prospectively with 50 in each group.

AGE DISTRIBUTION OF PATIENTS:

TABLE 5. AGE DISTRIBUTION OF PATIENTS IN GROUP C

GROUP C	AGE GROUPS				
	18-36	37-54	55-72	73-90	TOTAL
NUMBER	6	20	22	2	50
% OF TOTAL	12%	40%	44%	2%	100%

TABLE 6. AGE DISTRIBUTION OF PATIENTS IN GROUP T

GROUP T	AGE GROUPS				
	18-36	37-54	55-72	73-90	TOTAL
NUMBER	7	19	18	6	50
% OF TOTAL	14%	38%	36%	12%	100%

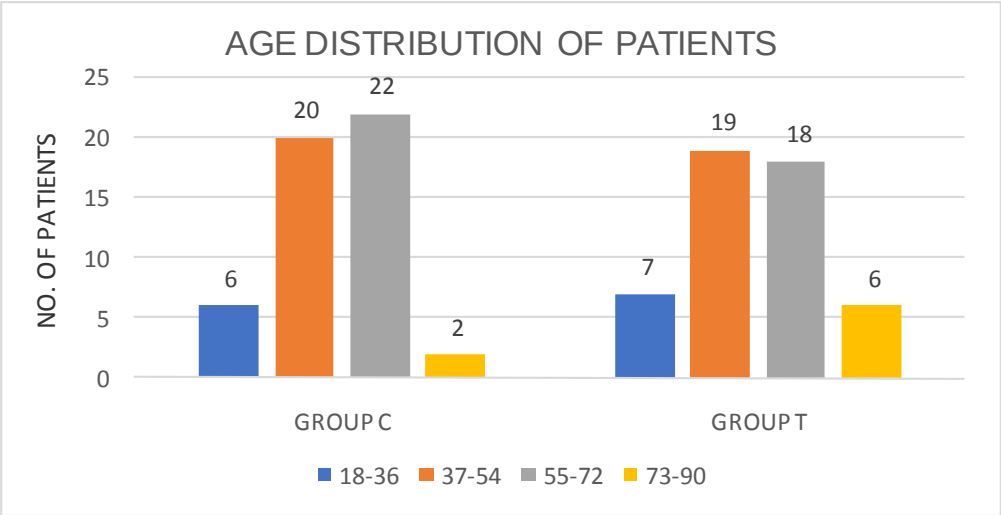
TABLE 7. MEAN AGE AMONG GROUPS

	GROUP C		GROUP T		Z	p-value
	Mean	SD	Mean	SD		
Age	50.64	14.62	54.12	15.10	-1.171	0.245

TABLE 8. MEDIAN AGE AMONG GROUPS

	GROUP C		GROUP T		Z	p-value
	Median	IQR	Median	IQR		
Age	54.00	38-61	52.5	41.75-67.25	-1.171	0.245

FIGURE 12. AGE DISTRIBUTION OF PATIENTS



Out of the 50 patients in group C, 14% (n=7) of patients were in the age group of 18-36 yrs., 38% (n= 19) belonged to 37-54 yrs. age group, 36 % (n=18) belonged to 55-72 yrs. age group and 12% (n = 6) belonged to 73-90 yrs. age group. The mean age of group C patients was 50.64±14.62 and the median age 54.00 (IQR:38-61).

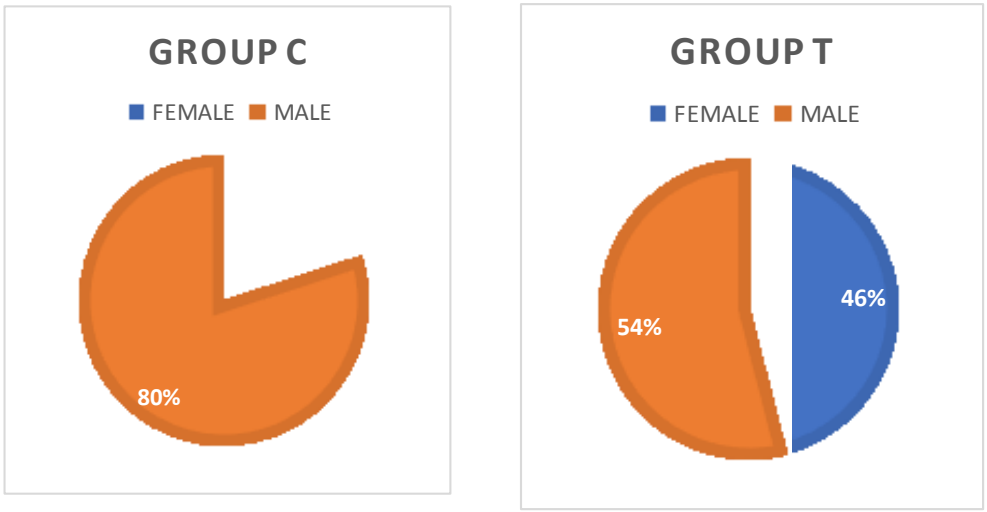
Out of the 50 patients in group T, 12% (n=6) of patients were in the age group of 18-36 yrs., 40% (n= 20) belonged to 37-54 yrs. age group, 44 % (n=22) belonged to 55-72 yrs. age group and 2% (n = 2) belonged to 73-90 yrs. age group. The mean age of group T patients was 54.12±15.10 and the median age 52.5 (IQR: 41.75-67.25). There was no statistically significant difference in the age distribution of both groups (p-value = 0.245)

SEX DISTRIBUTION OF PATIENTS:

TABLE 9. GENDER DISTRIBUTION AMONG GROUPS

SEX	GROUP C		GROUP T		Total	Chi-square value	p-value
	No. of cases	% of total	No. of cases	% of total			
F	10	20%	23	46%	33	7.644	0.006
M	40	80%	27	54%	67		
Total	50	100%	50	100%	100		

FIGURE 13. SEX DISTRIBUTION OF PATIENTS



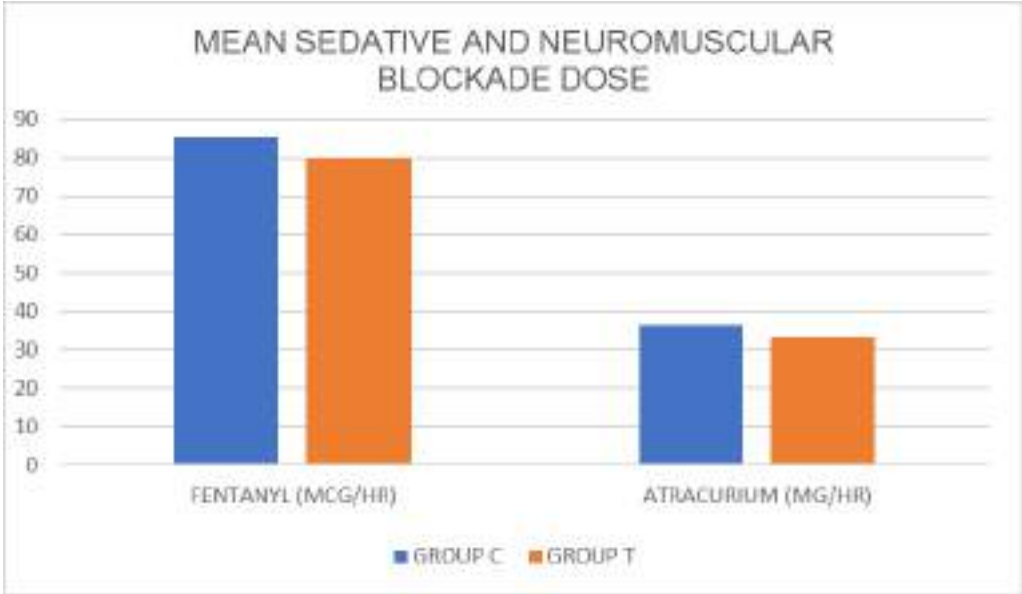
Out of the 50 patients included in group C, 10 were female and 40 were male whereas in group T 23 were female and 27 were male respectively. There was a statistically significant difference in the gender distribution between both groups (p-value = 0.006)

SEDATIVE AND NEUROMUSCULAR DOSE:

TABLE 10. MEAN SEDATIVE AND NMB DOSE AMONG GROUPS

DRUG	GROUP C		GROUP T		Z	p-value
Fentanyl dose (mcg/hr)	Mean	SD	Mean	SD	3.764	<0.001
	85.40	10.14	80.00	0.00		
NMB dose	GROUP C		GROUP T		Z	p-value
Atracurium dose (mg/hr)	Mean	SD	Mean	SD	2.527	0.013
	36.60	8.95	33.00	4.63		

FIGURE 14. MEAN SEDATIVE AND NEUROMUSCULAR BLOCKADE DOSE



The mean dose of fentanyl in group C and T were 85.4±10.14 and 80 mcg/hr. respectively. There was a statistically significant difference between sedative requirements between both groups (p-value < 0.001).

The mean dose of atracurium in groups C and T were 36.6±8.95 and 80±4.63 mg/hr. respectively. There was a statistically significant difference between neuromuscular blockade dose requirements between both groups (p-value = 0.013).

TABLE 11. COMPARISON OF BASELINE VENTILATOR PARAMETERS AMONG BOTH GROUPS

BASELINE VENTILATOR PARAMETERS	GROUP C		GROUP T		Z	p-value
	Mean	SD	Mean	SD		
FIO_2	0.97	0.07	0.89	0.18	2.863	0.005
TV (ml)	409.50	12.26	430.00	16.75	-6.983	<0.001
RATE	21.72	1.07	20.80	2.74	2.211	0.029
PEEP (cm of H_20)	10.80	1.28	12.28	2.28	-4.002	0.0001
Ti (s)	0.92	0.05	0.98	0.14	-2.760	0.007
PIP (cm of H_2O)	39.86	5.39	36.02	6.11	3.333	0.001
Pplat (cm of H_2O)	29.50	1.69	29.04	4.78	0.642	0.522
MAP (cm of H_2O)	26.28	2.52	20.04	4.12	9.148	<0.001
DP (cm of H_2O)	18.70	1.72	16.76	3.74	-3.329	0.0012
Respiratory System Compliance (ml/cm)	22.06	1.87	25.09	7.58	-2.744	0.007

TABLE 12. COMPARISON OF VENTILATOR PARAMETERS AMONG BOTH GROUPS AT 6 HOURS

VENTILATOR PARAMETERS	GROUP C		GROUP T		Z	p-value
	Mean	SD	Mean	SD		
FIO_2	0.95	0.08	0.90	0.16	2.124	0.036
TV (ml)	401.00	7.07	433	18.4	-11.479	<0.001
RATE	22.32	1.24	21.44	2.65	2.127	0.036
PEEP (cm of H_2O)	12.60	1.53	11.72	1.57	2.843	0.005
Ti (s)	0.90	0.05	0.95	0.13	-2.547	0.012
PPEAK (cm of H_2O)	38.96	4.38	37.12	5.82	1.786	0.077
Pplat (cm of H_2O)	29.52	1.43	29.58	4.15	-0.097	0.923
MAP (cm of H_2O)	24.86	2.34	21.18	2.83	7.083	<0.001
DP (cm of H_2O)	16.92	1.88	17.9	4.13	-1.527	0.1300
Respiratory system compliance (ml/cm)	23.97	2.49	25.7	7.08	-1.630	0.1063

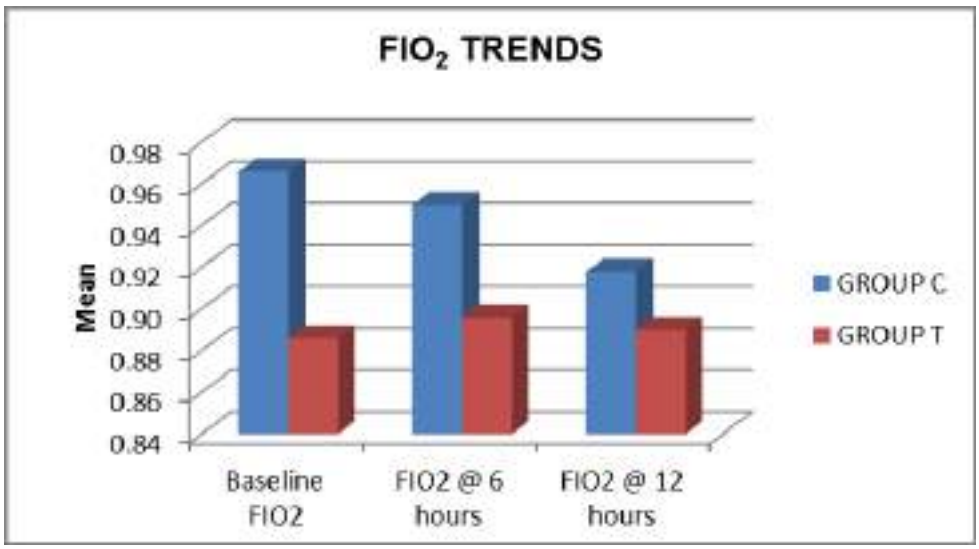
TABLE 13. COMPARISON OF VENTILATORY PARAMETERS AT 12 HOURS AMONG BOTH GROUPS

VENTILATOR PARAMETERS	GROUP C		GROUP T		Z	p-value
	Mean	SD	Mean	SD		
FIO_2	0.92	0.10	0.89	0.16	1.051	0.296
TV (ml)	401.00	7.07	432.50	18.39	-11.308	<0.001
RATE	22.68	1.38	22.32	3.41	0.692	0.491
PEEP (cm of H_2O)	13.24	1.06	12.88	1.81	1.212	0.229
Ti (s)	0.89	0.06	0.92	0.15	-1.455	0.149
PIP (cm of H_2O)	39.58	5.94	37.98	5.80	1.362	0.176
Pplat (cm of H_2O)	29.02	1.95	30.32	4.32	-1.938	0.055
MAP (cm of H_2O)	24.80	3.64	22.80	3.10	2.958	0.004
DP (cm of H_2O)	15.78	2.36	17.44	3.54	-2.759	0.007
RESPIRATORY SYSTEM COMPLIANCE (ml/cm of H_2O)	26.07	4.65	26.075	6.729	-0.004	0.996

TABLE 14. COMPARISON OF MEAN FiO_2 AMONG GROUPS

FiO_2	GROUP C	GROUP T
Baseline FiO_2	0.97	0.89
FiO_2 @ 6 hours	0.95	0.90
FiO_2 @ 12 hours	0.92	0.89

FIGURE 15. FiO_2 TRENDS ACROSS GROUPS

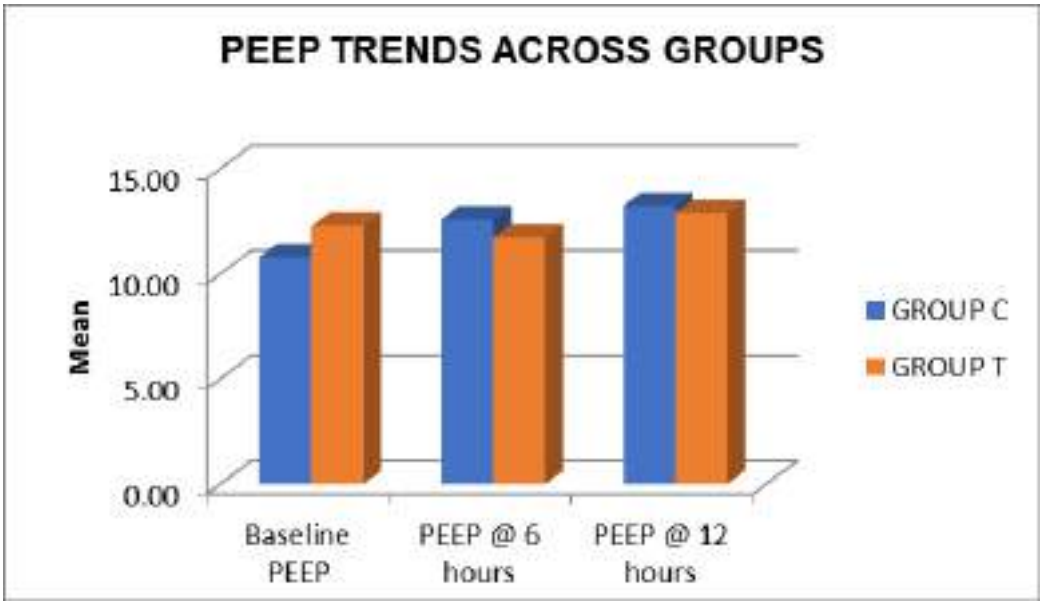


The mean FiO_2 in group C at baseline, at 6 hours and 12 hours was 0.97, 0.95 and 0.92 respectively whereas the mean FiO2 in group T at baseline, at 6 hours and 12 hours was 0.89, 0.90 and 0.89 respectively. The mean FiO_2 used was slightly higher in group C at baseline (p-value: 0.005), 6 hours (p-value: 0.036) and at 12 hours (p-value: 0.296) compared to group T.

TABLE 15. COMPARISON OF MEAN PEEP AMONG GROUPS

PEEP	GROUP C	GROUP T
Baseline PEEP	10.80	12.28
PEEP @ 6 hours	12.60	11.72
PEEP @ 12 hours	13.24	12.88

FIGURE 16. PEEP TRENDS ACROSS GROUPS

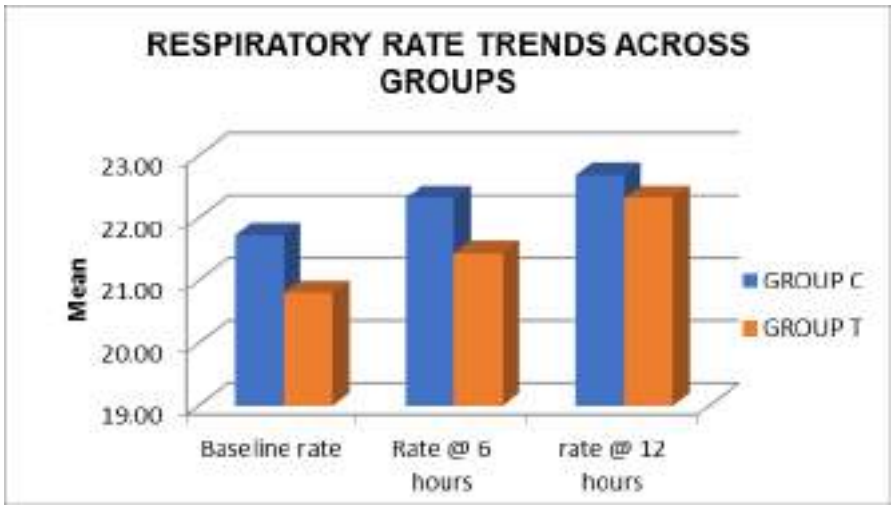


The mean PEEP in group C at baseline, at 6 hours and 12 hours was 10.8, 12.6 and 13.24 cm of H_2O respectively whereas the mean PEEP in group T at baseline, at 6 hours and 12 hours was 12.28, 11.72 and 12.88 cm of H_2O respectively. The mean PEEP used was slightly lower in group C at baseline (p-value: 0.0001) and higher at 6 hours (p-value: 0.005) and at 12 hours (p-value: 0.229) compared to group T.

TABLE 16. COMPARISON OF MEAN RESPIRATORY RATE ACROSS GROUPS

Respiratory rate	GROUP C	GROUP T
Baseline rate	21.72	20.80
Rate @ 6 hours	22.32	21.44
Rate @ 12 hours	22.68	22.32

FIGURE 17. RESPIRATORY RATE TRENDS ACROSS GROUPS

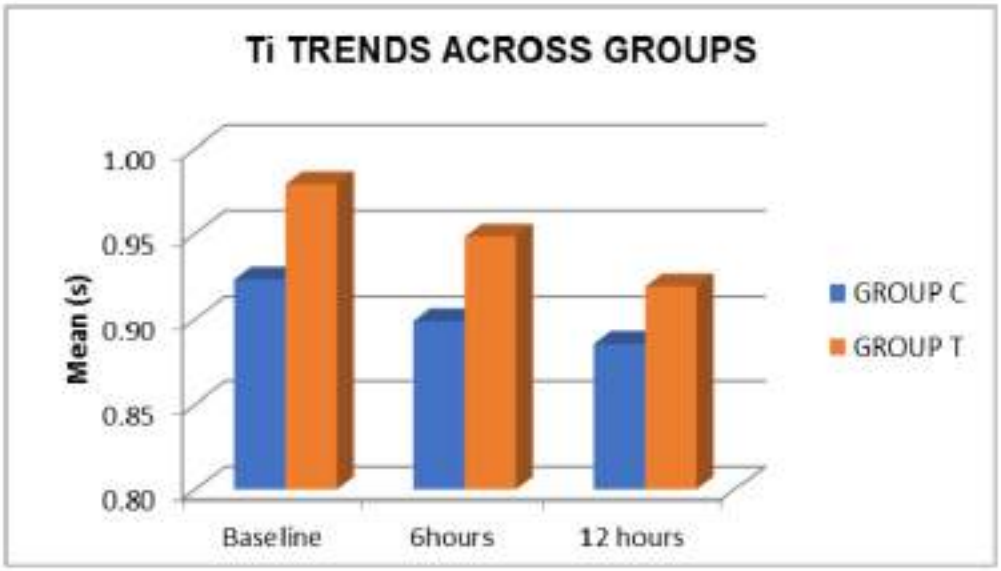


The mean respiratory rate in group C at baseline, at 6 hours and 12 hours was 21.72, 22.32 and 22.68 respectively whereas the mean respiratory rate in group T at baseline, at 6 hours and 12 hours was 20.88, 21.44 and 22.32 respectively. The mean respiratory rate was slightly higher in group C at baseline (p-value: 0.029) at 6 hours (p-value: 0.036) and 12 hours (p-value: 0.491) compared to group T.

TABLE 17. COMPARISON OF MEAN Ti ACROSS GROUPS

Inspiratory time (s)	GROUP C	GROUP T
Baseline	0.92	0.98
6 hours	0.90	0.95
12 hours	0.89	0.92

FIGURE 18. Ti TRENDS ACROSS GROUPS

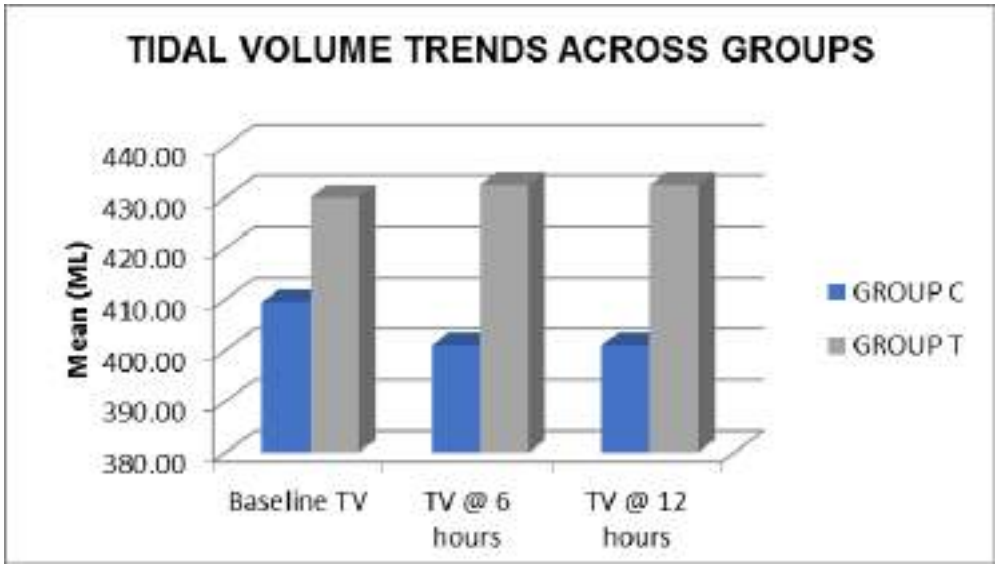


The mean inspiratory time (Ti) in group C at baseline, at 6 hours and 12 hours was 0.92s, 0.90s and 0.89s respectively whereas the mean inspiratory time in group T at baseline, at 6 hours and 12 hours was 0.98s, 0.95s and 0.92s respectively. The mean inspiratory time was slightly higher in group T at baseline (p-value: 0.0007) at 6 hours (p-value: 0.012) and 12 hours (p-value: 0.149) compared to group T.

TABLE 18. COMPARISON OF MEAN TIDAL VOLUME ACROSS GROUPS

Tidal volume	GROUP C	GROUP T
Baseline TV	409.50	430
TV @ 6 hours	401.00	433
TV @ 12 hours	401.00	432.50

FIGURE 19. TIDAL VOLUME TRENDS ACROSS GROUPS

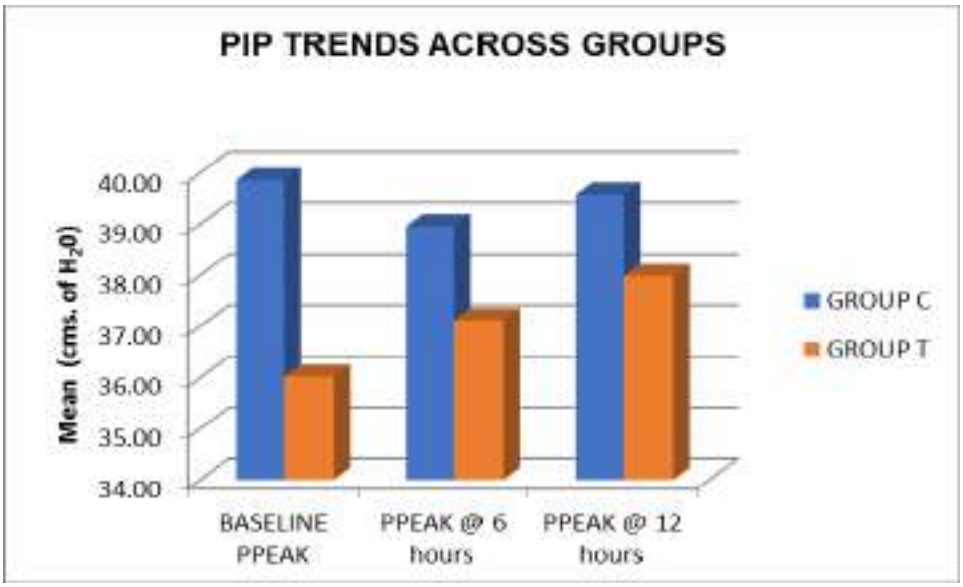


The mean Tidal volume in group C at baseline, at 6 hours and 12 hours was 409.5, 401 and 401ml respectively whereas the mean Tidal volume time in group T at baseline, at 6 hours and 12 hours was 430, 4323 and 432.5 ml respectively. The mean Tidal volume was slightly higher in group T at baseline (p-value: <0.001) at 6 hours (p-value: <0.001) and at 12 hours (p-value: <0.001) compared to group T.

TABLE 19. COMPARISON OF MEAN PEAK INSPIRATORY PRESSURE ACROSS GROUPS

PEAK INSPIRATORY PRESSURE (PIP)	GROUP C	GROUP T
Baseline PIP	39.86	36.02
PIP @ 6 hours	38.96	37.12
PIP @ 12 hours	39.58	37.98

FIGURE 20. PIP TRENDS ACROSS GROUPS

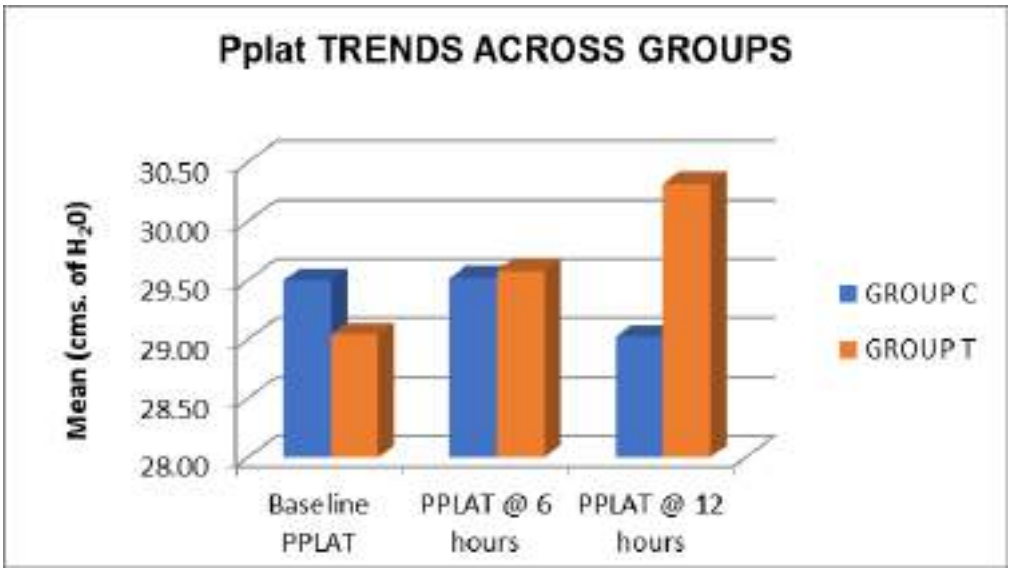


The mean PIP in group C at baseline, at 6 hours and 12 hours was 39.86, 38.96 and 39.58 cm of H_2O respectively whereas the mean PIP in group T at baseline, at 6 hours and 12 hours was 36.02, 37.12 and 37.98 cm of H_2O respectively. The mean PIP was slightly higher in group C at baseline (p-value: 0.001), at 6 hours (p-value: 0.077) and 12 hours (p-value: 0.176) compared to group T.

TABLE 20. COMPARISON OF MEAN PLATEAU PRESSURE ACROSS GROUPS

PLATEAU PRESSURE	GROUP C	GROUP T
Baseline Pplat	29.50	29.04
Pplat @ 6 hours	29.52	29.58
Pplat @ 12 hours	29.02	30.32

FIGURE 21. Pplat TRENDS ACROSS GROUPS

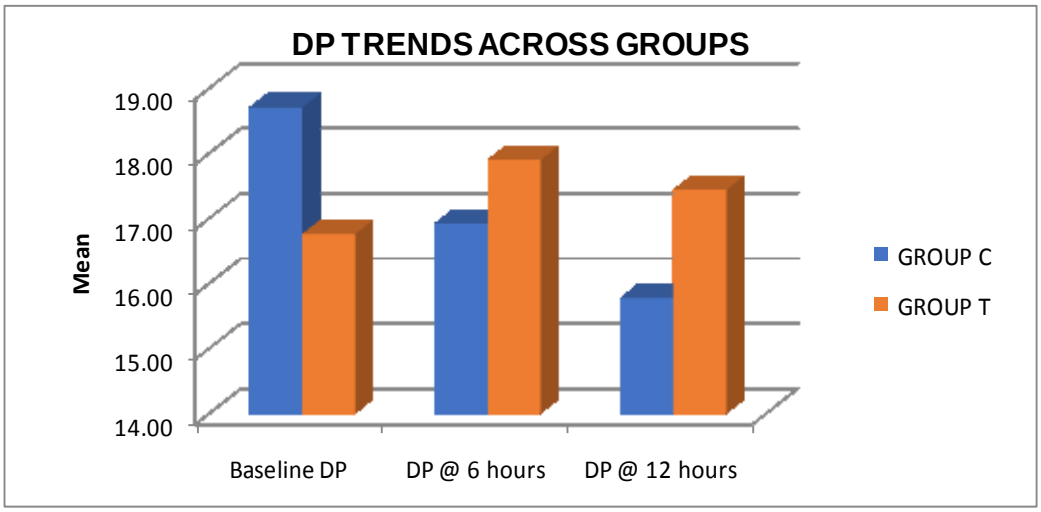


The mean Pplat in group C at baseline, at 6 hours and 12 hours was 29.50, 29.52 and 29.02 cm of H_2O respectively whereas the mean Pplat in group T at baseline, at 6 hours and 12 hours was 29.04, 29.58 and 30.32 cm of H_2O respectively. The mean Pplat was slightly higher in group C at baseline (p-value: 0.522) and lower at 6 hours (p-value: 0.923) and 12 hours (p-value: 0.055) compared to group T.

TABLE 21. COMPARISON OF MEAN DRIVING PRESSURE ACROSS GROUPS

DRIVING PRESSURE	GROUP C	GROUP T
Baseline DP	18.70	16.76
DP @ 6 hours	16.92	17.9
DP @ 12 hours	15.78	17.44

FIGURE 22. DP TRENDS ACROSS GROUPS

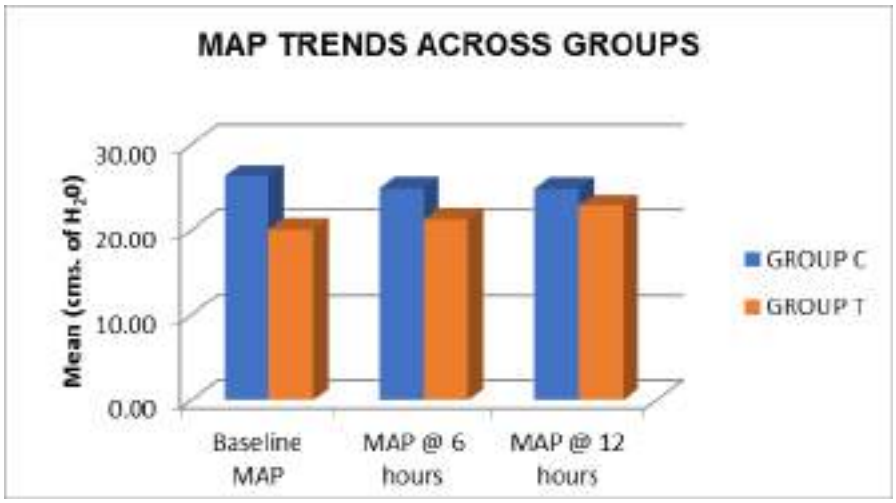


The mean DP in group C at baseline, at 6 hours and 12 hours was 18.7, 16.92 and 15.78 cm of H_2O respectively whereas the mean DP in group T at baseline, at 6 hours and 12 hours was 16.76, 17.9 and 17.44 cm of H_2O respectively. The mean DP was slightly higher in group C at baseline (p-value: 0.001) and lower at 6 hours (p-value: 0.13) and 12 hours (p-value: 0.007) compared to group T.

TABLE 22. COMPARISON OF MEAN AIRWAY PRESSURE ACROSS GROUPS

MEAN AIRWAY PRESSURE	GROUP C	GROUP T
Baseline MAP	26.28	20.04
MAP @ 6 hours	24.86	21.18
MAP @ 12 hours	24.80	22.80

FIGURE 23. MAP TRENDS ACROSS GROUPS

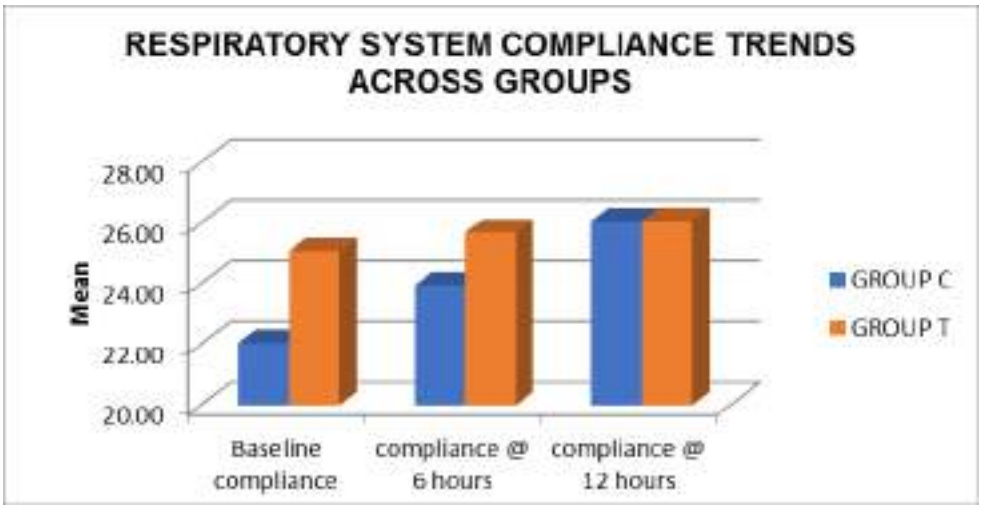


The mean MAP in group C at baseline, at 6 hours and 12 hours was 26.2, 24.86 and 24.8 cm of H_2O respectively whereas the mean MAP in group T at baseline, at 6 hours and 12 hours was 20.04, 21.18 and 22.8 cm of H_2O respectively. The mean MAP was slightly higher in group C at baseline (p-value: <0.001), at 6 hours (p-value: <0.001) and at 12 hours (p-value: 0.004) compared to group T.

TABLE 23. COMPARISON OF RESPIRATORY SYSTEM COMPLIANCE ACROSS GROUPS

RESPIRATORY SYSTEM COMPLIANCE(ml/cm of H_2O)	GROUP C	GROUP T
Baseline compliance	22.06	25.09
Compliance @ 6 hours	23.97	25.7
Compliance @ 12 hours	26.07	26.075

FIGURE 24. RESPIRATORY SYSTEM COMPLIANCE TRENDS ACROSS GROUPS

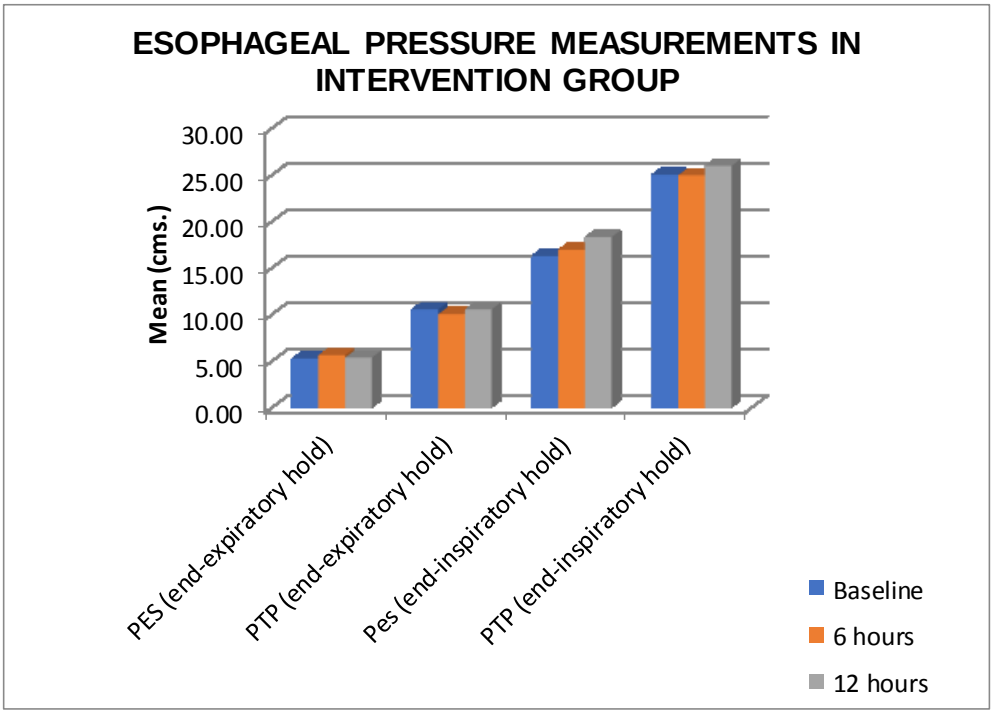


The mean respiratory system compliance in group C at baseline, at 6 hours and 12 hours was 22.06, 23.97 and 26.07 ml/cm of H_2O respectively whereas the mean respiratory system compliance in group T at baseline, at 6 hours and 12 hours was 25.09, 25.7 and 26.075 ml/cm of H_2O respectively. The mean respiratory system compliance was slightly lower in group C at baseline (p-value: 0.008), at 6 hours (p-value: 0.298) and higher at 12 hours (p-value: 0.835) compared to group T.

TABLE 24. COMPARISON OF MEAN ESOPHAGEAL AND TRANSPULMONARY PRESSURES IN INTERVENTION GROUP

	Baseline	6 hours	12 hours
Pes (end-expiratory hold)	5.30	5.66	5.40
PTP (end-expiratory hold)	10.6	10.08	10.60
Pes (end-inspiratory hold)	16.32	16.98	18.36
PTP (end-inspiratory hold)	25.04	25.00	26.00

FIGURE 25. ESOPHAGEAL PRESSURE MEASUREMENTS IN INTERVENTION GROUP

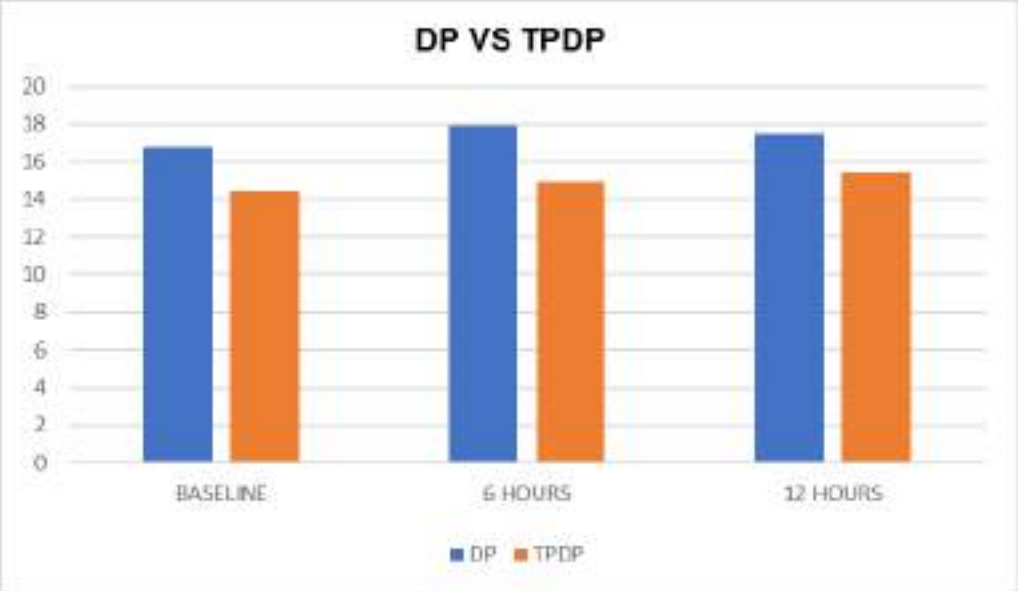


The mean PES (end-expiratory hold) in group T at baseline, at 6 hours and 12 hours was 5.3, 5.66 and 5.4 cm of H_2O respectively. The mean PTP (end-expiratory hold) in group T at baseline, at 6 hours and 12 hours was 11, 10.6 and 10.6 cm of H_2O respectively. The Pes (end-inspiratory hold) in group T at baseline, at 6 hours and 12 hours was 16.32, 16.38 and 18.36 cm of H_2O respectively compared to group T.

TABLE 25. COMPARISON OF DRIVING PRESSURE AND TRANSPULMONARY DRIVING PRESSURE IN INTERVENTION GROUP

TIME	DP (cm)		TPDP (cm)			
	mean	SD	mean	SD	z value	p-value
Baseline	16.76	3.744	14.44	3.9494	3.014	0.0033
At 6 hours	17.9	4.13	14.92	3.1157	4.073	0.0001
At 12 hours	17.44	3.59	15.4	2.806	3.166	0.002

FIGURE 26. DRIVING PRESSURE VS TRANSPULMONARY DRIVING PRESSURE



The transpulmonary measured DP was 14.44, 14.92 and 15.4 cm of H_2O at baseline, 6 hours and 12 hours respectively. The transpulmonary measured DP was lower compared to the normal DP at baseline (p-value: 0.003), 6 hours (p-value: 0001) and 12 hours (p-value: 0.002).

TABLE 26. ABG VALUES AT BASELINE AMONG GROUPS

ABG VALUES	GROUP C		GROUP T		Z	p-value
	Mean	SD	Mean	SD		
pH	7.27	0.09	7.20	0.25	2.126	0.036
PaO_2	75.12	27.74	64.10	21.52	2.219	0.029
$PaCO_2$	47.92	14.03	54.18	17.28	-1.989	0.049
HCO_3	23.44	7.31	19.78	6.13	2.713	0.008
PaO_2/FiO_2	77.97	27.68	79.72	44.22	-0.238	0.813
A-a	554.06	54.11	489.84	58.39	5.704	0.001
a/A	0.12	0.04	0.12	0.04	0.262	0.794

TABLE 27. ABG VALUES AT 6 HOURS AMONG GROUPS

ABG VALUES	GROUP C		GROUP T		Z	p-value
	Mean	SD	Mean	SD		
pH	7.26	0.13	7.25	0.18	0.220	0.826
PaO_2	73.30	21.50	70.54	20.04	0.664	0.508
$PaCO_2$	47.98	12.75	47.32	13.12	0.255	0.799
HCO_3	22.91	7.25	20.08	5.61	2.185	0.031
pH	594.88	69.67	576.35	107.65	1.022	0.309

TABLE 28. ABG VALUES AT 12 HOURS AMONG GROUPS

ABG VALUES	GROUP C		GROUP T		Z	p-value
	Mean	SD	Mean	SD		
pH	7.31	0.13	7.28	0.17	0.788	0.433
PaO_2	81.68	27.69	77.90	17.84	0.811	0.419
$PaCO_2$	47.72	16.12	46.58	10.95	0.414	0.680
HCO_3	23.16	6.60	20.75	5.41	1.993	0.049
PaO_2/FiO_2	91.45	36.10	94.06	42.09	-0.332	0.740
A-a	513.20	80.00	498.45	118.00	0.732	0.466
a/A	0.14	0.05	0.15	0.07	-0.445	0.657

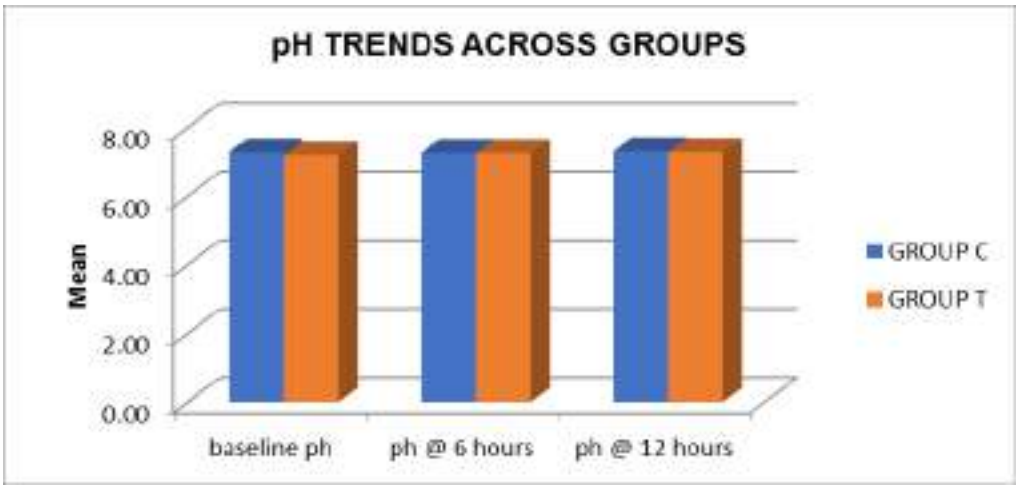
TABLE 29. COMPARISON OF OXYGENATION AND CO_2 GRADIENTS AMONG GROUPS

OXYGENATION AND CO_2 GRADIENTS	GROUP C		GROUP T		Z	p-value
	Mean	SD	Mean	SD		
$\Delta paCO_2$ @ 12 hours	-0.20	5.18	-7.60	14.48	3.403	0.001
ΔHCO_3 @ 12 hours	-0.29	2.87	0.97	4.52	-1.656	0.101
$\Delta PaO_2/FiO_2$ @ 12 hours	13.48	29.12	14.34	15.60	-0.183	0.855
ΔA-a @ 12 hours	-40.85	67.94	8.61	125.54	-2.450	0.016
Δa/A @ 12 hours	0.02	0.04	0.03	0.05	-0.794	0.429

TABLE 30. COMPARISON OF MEAN pH AMONG GROUPS

pH	GROUP C	GROUP T
Baseline pH	7.27	7.20
pH @ 6 hours	7.26	7.25
pH@ 12 hours	7.31	7.28

FIGURE 27. pH TRENDS ACROSS GROUPS

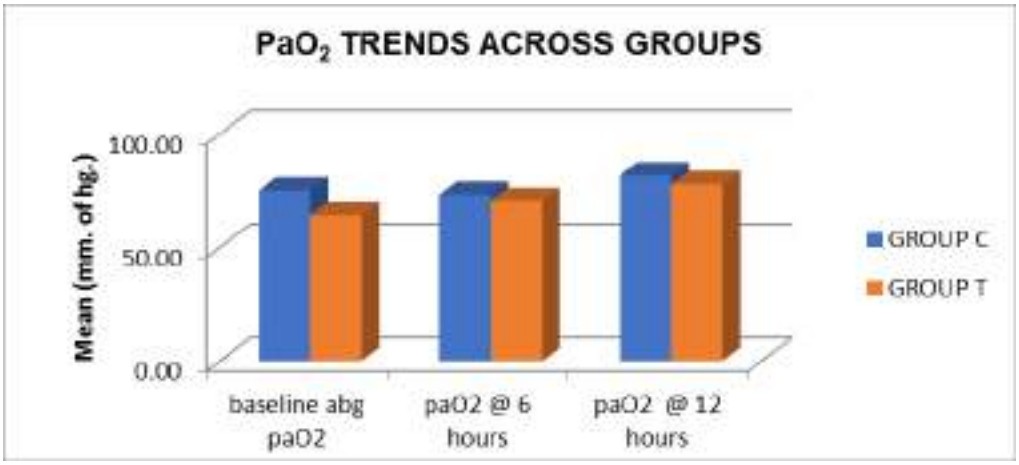


The mean pH in group C at baseline, at 6 hours and 12 hours was 7.27, 7.26 and 7.31 respectively whereas the mean pH in group T at baseline, at 6 hours and 12 hours was 7.2, 7.25 and 7.28 respectively. The mean pH was slightly higher in group C at baseline (p-value: 0.036), 6 hours (p-value: 0.826) and 12 hours (p-value: 0.433) compared to group T.

TABLE 31. COMPARISON OF MEAN PaO_2 AMONG GROUPS

PaO_2	GROUP C	GROUP T
Baseline	75.12	64.10
PaO_2 @ 6 hours	73.30	70.54
PaO_2 @ 12 hours	81.68	77.90

FIGURE 28. PaO_2 TRENDS ACROSS GROUPS

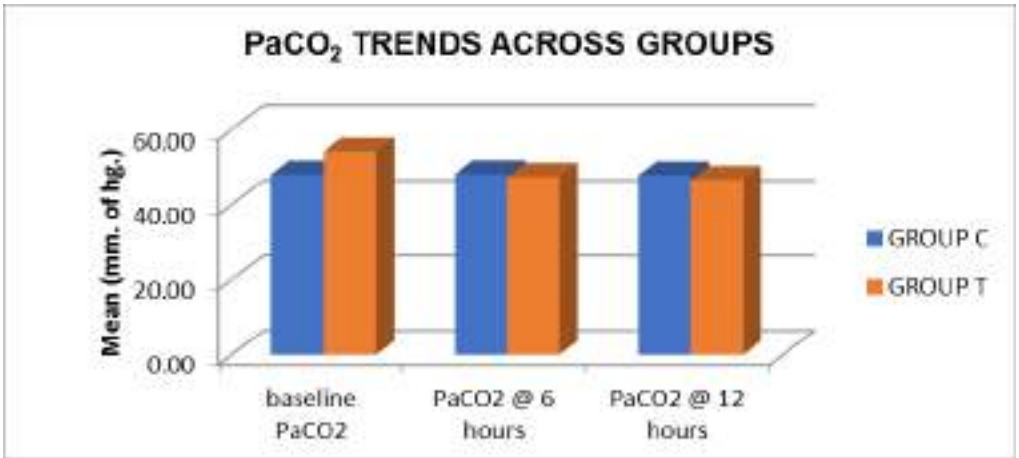


The mean PaO_2 in group C at baseline, at 6 hours and 12 hours was 75.12, 73.3 and 81.68 mm. of Hg. respectively whereas the mean PaO_2 in group T at baseline, at 6 hours and 12 hours was 64.1, 70.54 and 77.9 mm. of Hg. respectively. The mean PaO_2 was slightly higher in group C at baseline (p-value: 0.029), 6 hours (p-value: 0.508) and 12 hours (p-value: 0.419) compared to group T.

TABLE 32. COMPARISON OF MEAN $PaCO_2$ AMONG GROUPS

$PaCO_2$	GROUP C	GROUP T
Baseline $PaCO_2$	47.92	54.18
$PaCO_2$ @ 6 hours	47.98	47.32
$PaCO_2$ @ 12 hours	47.72	46.58

FIGURE 29. $PaCO_2$ TRENDS ACROSS GROUPS

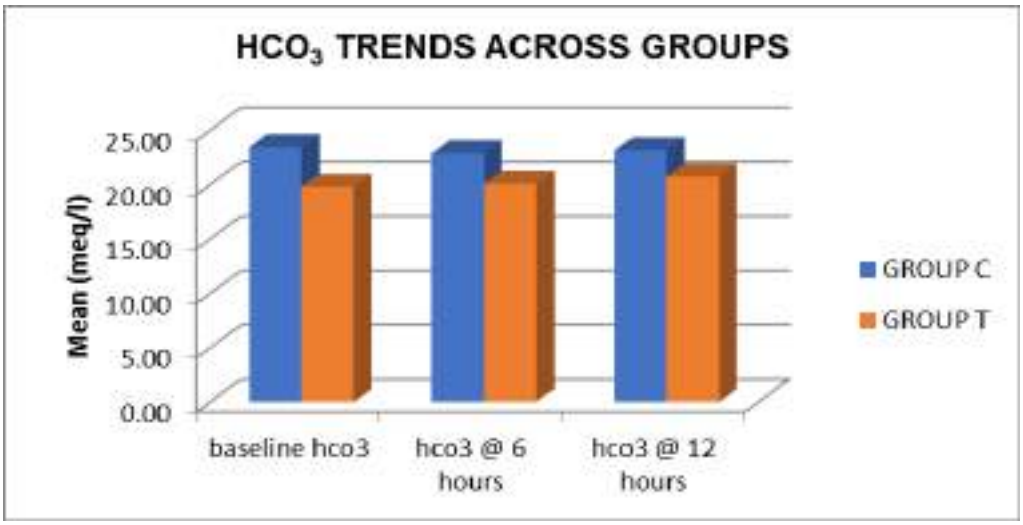


The mean $PaCO_2$ in group C at baseline, at 6 hours and 12 hours was 47.92, 47.98 and 47.72 mm. of Hg. respectively whereas the mean $paCO_2$ in group T at baseline, at 6 hours and 12 hours was 54.18, 47.32 and 46.58 mm. of Hg. respectively. The mean $PaCO_2$ was slightly lower in group C at baseline (p-value: 0.049) and higher at 6 hours (p-value: 0.799) and 12 hours (p-value: 0.680) compared to group T.

TABLE 33. COMPARISON OF MEAN HCO_3 AMONG GROUPS

HCO_3	GROUP C	GROUP T
Baseline HCO_3	23.44	19.78
HCO_3 @ 6 hours	22.91	20.08
HCO_3 @ 12 hours	23.16	20.75

FIGURE 30. HCO_3 TRENDS ACROSS GROUPS

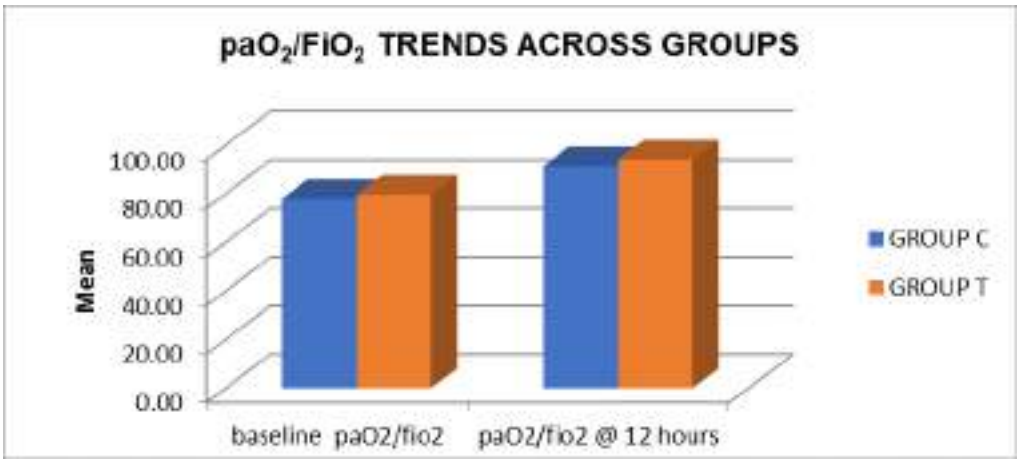


The mean HCO_3 in group C at baseline, at 6 hours and 12 hours was 23.44, 22.91 and 23.16 mEq/l respectively whereas the mean $paCO_2$ in group T at baseline, at 6 hours and 12 hours was 19.78, 20.08 and 20.75 mEq/l respectively. The mean HCO_3 was slightly higher in group C at baseline (p-value: 0.008) at 6 hours (p-value: 0.031) and 12 hours (p-value: 0.049) compared to group T.

TABLE 34. COMPARISON OF MEAN PaO2/FiO$_2$ AMONG GROUPS

PaO_2/FiO_2	GROUP C	GROUP T
Baseline PaO_2/FiO_2	77.97	79.72
PaO_2/FiO_2 @ 12 hours	91.45	94.06

FIGURE 31. PaO_2/FiO_2 TRENDS ACROSS GROUPS



The mean PaO_2/FiO_2 in group C at baseline and 12 hours was 77.97 and 91.45 respectively whereas the mean PaO_2/FiO_2 in group T at baseline and 12 hours was 79.72 and 94.06. The mean PaO2/FiO$_2$ was slightly lower in group C at baseline (p-value: 0.813) and 12 hours (p-value: 0.740) compared to group T.

TABLE 35. COMPARISON OF MEAN ALVEOLAR AND ARTERIAL GRADIENTS AMONG GROUPS

ALVEOLAR AND ARTERIAL GRADEINTS	GROUP C	GROUP T
Baseline A-a	554.06	489.84
A-a @ 12 hours	513.20	498.45
Baseline a/A	0.12	0.12
a/A @ 12 hours	0.14	0.15

FIGURE 32. A-a TRENDS ACROSS GROUPS

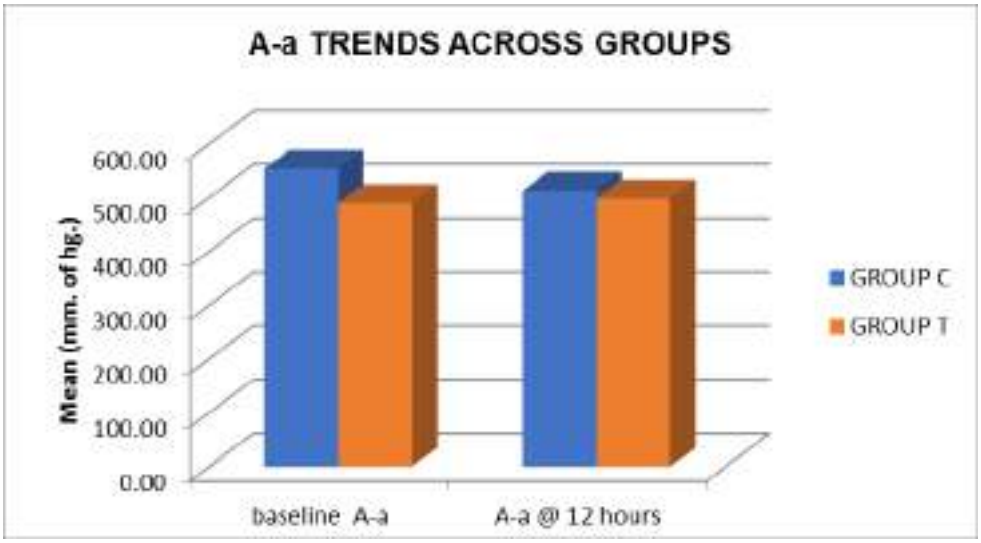
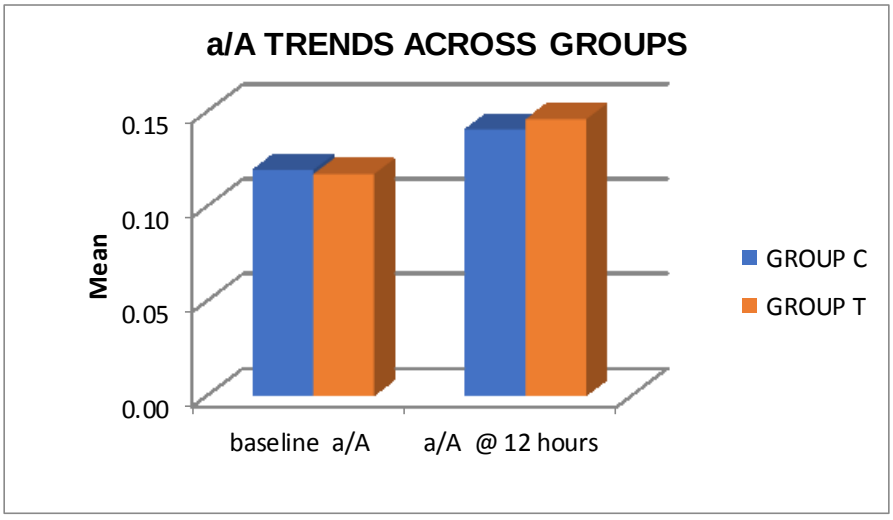


FIGURE 33. a/A TRENDS ACROSS GROUPS



The mean A-a gradient in group C at baseline and 12 hours was 554.06 and 513.2 mm. of Hg respectively whereas the mean A-a gradient in group T at baseline and 12 hours was 489.06 and 498.45 mm. of Hg. The mean A-a gradient was higher in group C at baseline (p-value: 0.001) and 12 hours (p-value: 0.466) compared to group T.

The mean a/A in group C at baseline and 12 hours was 0.12 and 0.14 respectively whereas the mean a/A in group T at baseline and 12 hours was 0.12 and 0.15. The mean a/A was the same in both groups at baseline (p-value: 0.794) but was lower in group C at 12 hours (p-value: 0.657) compared to group T.

TABLE 36. COMPARISON OF OXYGENATION AND CO_2 GRADIENTS AMONG GROUPS

OXYGENATION AND CO_2 GRADIENTS	GROUP C	GROUP T
$\Delta PaCO_2$ @ 12 hours	-0.20	-7.60
ΔHCO_3 @ 12 hours	-0.29	0.97
$\Delta PaO_2/FiO_2$ @ 12 hours	13.48	14.34
ΔA-a @ 12 hours	-40.85	8.61
Δa/A @ 12 hours	0.02	0.03

The mean $\Delta PaCO_2$ in group C at 12 hours was -0.20 mm. of Hg and Δhco3 was -0.29mEq/l respectively whereas the mean ΔpCO_2 in group T at 12 hours was -7.60. of Hg and ΔHCO_3 was 0.97 mEq/l respectively. the mean $\Delta PaCO_2$ (p-value: 0.001) and ΔHCO_3 (p-value: 0.101) was higher in group T at 12 hours compared to group C.

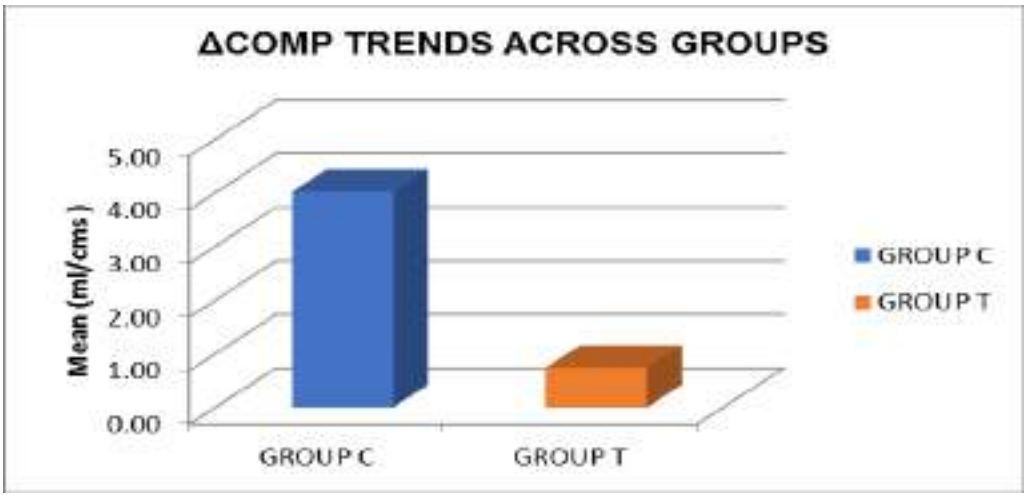
The mean ΔA-a gradient in group C at 12 hours was -40.65 mm. of Hg and Δa/A was 0.02 respectively whereas the mean ΔA-a gradient in group T at 12 hours was 8.61 mm. of Hg and Δa/A was 0.03 respectively. the mean ΔA-a was higher in group C compared to group T (p-value: 0.016) and Δa/A (p-value: 0.429) was higher in group T at 12 hours compared to group C.

The mean $\Delta PaO_2/FiO_2$ in group C at 12 hours was 13.48 whereas the mean PaO_2/FiO_2 in group T at 12 hours was 14.34. The mean PaO_2/FiO_2 was slightly lower in group C at 12 hours (p-value: 0.855) compared to group T.

TABLE 37. COMPARISON OF ΔCOMP ACROSS GROUPS

ΔCOMP	GROUP C		GROUP T		Z	p-value
	Mean	SD	Mean	SD		
ΔCOMP at 12 hours	4.01	3.81	-1.17	2.7	7.844	<0.001

FIGURE 34. ΔCOMP TRENDS ACROSS GROUPS

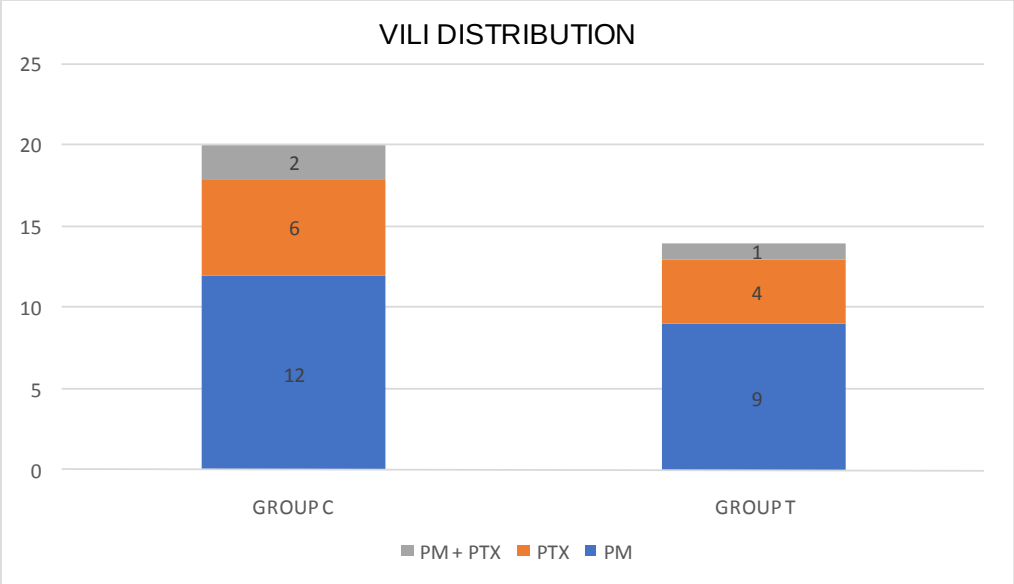


The mean ΔCOMP (change in compliance) at 12 hours in group C was 4 ml/cm of H_2O whereas in group T was -1.17 ml/cm of H_2O. The mean ΔCOMP was higher in group C compared to group T (p-value:<0.001)

TABLE 38. VILI DISTRIBUTION ACROSS GROUPS

VILI	GROUP C		GROUP T		Total	Chi-square value	p-value
	No. of cases	%age	No. of cases	%age			
PM	12	60%	9	64%	21	0.106	0.948
PTX	6	30%	4	29%	10		
PTX & PM	2	10%	1	7%	3		
total	20	100%	14	100%	34		

FIGURE 35. VILI DISTRIBUTION ACROSS GROUPS



A Total of 20 patients had VILI in group C. 12 patients (60%) had pneumomediastinum, 6(30%) had a pneumothorax and 2(10%) had both pneumomediastinum and pneumothorax. A Total of 14 patients had VILI in group C. 9 patients (64%) had pneumomediastinum, 4(29%) had a pneumothorax and 1(7%) had both pneumomediastinum and pneumothorax. There was no statistically significant difference in VILI in between both groups.

DISCUSSION

There has been a rise in the incidence of ARDS particularly with the onset of the COVID-19 pandemic and the mortality reaching up to 45% in ARDS and 59% in those requiring invasive mechanical ventilation.[1,2,58]

Many trials were conducted aiming at understanding the pathophysiology, biomechanical effects of invasive mechanical ventilation, benefits of adjunctive therapies including proning, extracorporeal therapies including $ECCO_2$ and Extracorporeal membrane oxygenation.[59,60]

Despite these advances, there is still no effective direct therapy for treating ARDS. Only lung-protective ventilation with low tidal volume and proning have shown benefit.[6,11] The optimal PEEP essential to maintain oxygenation with a lower incidence of VILI has also been investigated in the XPRESS, LOV and ALVEOLI studies.[38–40]They have failed to show any significant mortality benefit. Thus, in theory, optimal PEEP should be high enough to keep alveoli open and decrease regional mechanical heterogeneity while also sufficiently low to minimize overdistension of more compliant lung regions. In 2008 Talmor et al. used esophageal pressure guided ventilatory strategy and found improved compliance and oxygenation in the intervention group.[61]

In 2019, EPVENT-2, a large multicenter trial evaluated the same approach and found no statistical difference between barotrauma, shock-free days, acute kidney injury, PaO_2/FiO_2 ratio, PEEP and DP between the two groups.[62] Hence, we conducted a study in 100 patients in whom a esophageal pressure guided ventilatory strategy was compared with conventional ventilation for assessing benefits with regards to compliance, oxygenation and barotrauma.

In our study we enrolled 100 patients with 50 patients randomized to each group. Patients in both groups were comparable with similar

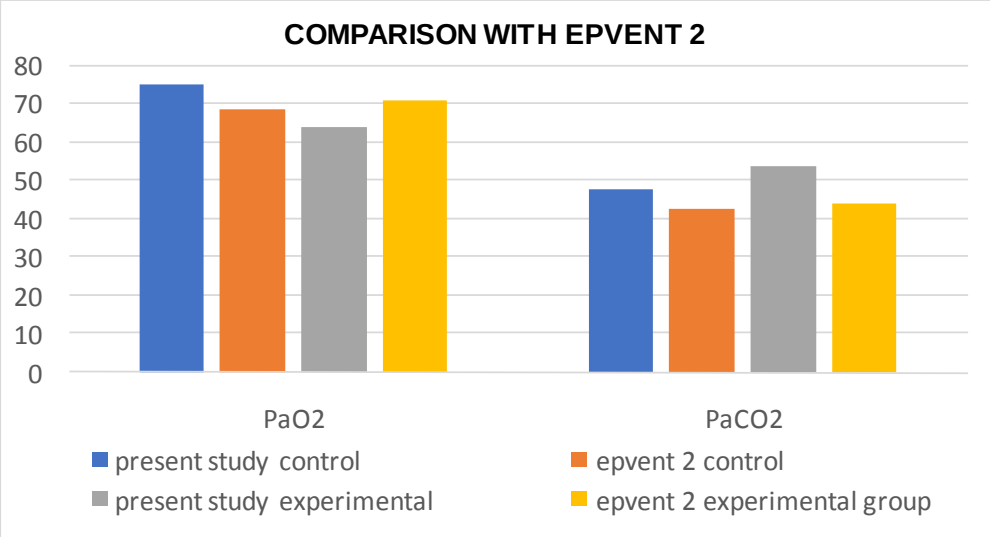
demographic, baseline characteristics, disease severity and ventilation requirement except gender. The mean age of group C patients was 50.64±14.62 and the mean age of group T patients was 54.12±15.10. There was no statistically significant difference in the age distribution of both groups (p-value = 0.245) which was in coherence with the EPVENT trial in which the mean age in the control and interventional arms were 51.2±23.0 and 54.5±16.1 years respectively.[61]

Male gender predominated both interventional and control groups constituting 80% and 54% respectively. Talmor et al also reported a similar distribution in their study.[61]

In our study at baseline, the mean FiO_2 (Table 14), respiratory rate (Table 16), Peak inspiratory pressure (Table 19), plateau pressure (Table 20), driving pressure (Table 21) in the control group were higher than the intervention group. However, tidal volume (Table 18), PEEP (Table 15), inspiratory time (Table 17) and respiratory system compliance (Table 23) were lower in the control group as compared to the interventional group. Our results are similar to the EPVENT 2 trial where the control group had lower respiratory system compliance, lower PEEP, lower plateau pressure and had higher driving pressure compared to the interventional group.[62]

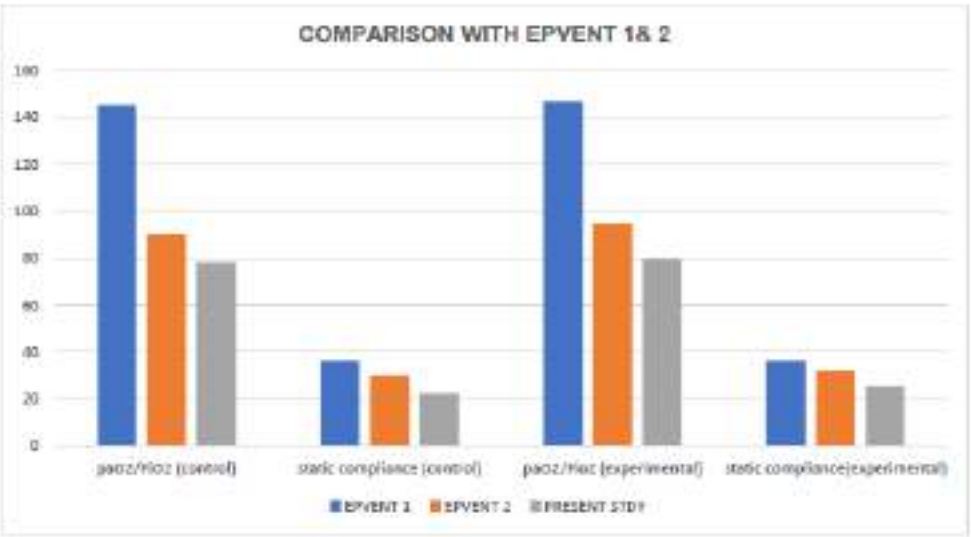
In our study at baseline, the mean pH, PaO_2, HCO_3 were lower and $paCO_2$ was higher in the interventional group compared to the control group. These results are also comparable to the EPVENT 2 trial where PaO_2 and $PaCO_2$ were lower in the control group compared to the interventional group.

FIGURE 36. COMPARISON WITH EPVENT 2 TRIAL



The PaO_2/FiO_2 was lower (77.97 vs 79.72) and the A-a gradient (554 vs. 490) was higher in the control group compared to the interventional group at baseline with the mean ratios being less than 100 in both the groups with the majority of patients having severe ARDS. However, in the EPVENT trial both the groups had near identical PaO_2/FiO_2 and a majority of patients in both the groups had moderate ARDS as compared to our patients who had severe ARDS.

FIGURE 37. COMPARISON WITH EPVENT 1& 2 TRIALS



At end of 12 hours, $\Delta PaCO_2$ was higher in the intervention group compared to the control group (p-value: 0.001) in the present study. $\Delta PaCO_2$ was not investigated in both EPVENT 1 and EPVENT 2 trials. The drop in $PaCO_2$ in our patients whose ventilation was guided by transpulmonary pressure can be explained probably by the improved dead space ventilation. However, High PEEP in the control group subset of COVID-19 patients who had low elastance might have accentuated stresses on highly permeable microvessels. This could have compromised CO_2 exchange without the benefit of widespread recruitment of functional lung units and thus $\Delta PaCO_2$ remained low in this group. Improvements in CO_2 exchange were probably because of improved dead space ventilation in the intervention arm. VILI was also lower in the intervention arm compared to the control arm.

At end of 12 hours, $\Delta PaO_2/FiO_2$ (p-value: 0.855) and Δa/A (p-value: 0.429) were slightly higher in the intervention group but were not statistically significant whereas improvement in the A-a gradient was higher in the control group though statistically not significant. Transpulmonary pressure guided ventilation lead to improvement in $PaO2/fiO_2$, and a/A ratios in the intervention group but was not statistically significant because of near similar PEEP levels in both groups and presence of more severe disease in the intervention arm. Improvements in respiratory system compliance in the control group compared to the intervention group were statistically significant but clinically non significant.

However, improvements in PaO_2/FiO_2 (p-value: 0.002) and compliance (p-value: 0.005) seen in the intervention arm in the EPVENT 1 trial were clinically and statistically significant. This can be due to the higher incidence of patients with moderate ARDS and predominance of secondary ARDS in the EPVENT 1 study population. In the present study, the peak inspiratory pressures were lower and plateau pressures were slightly higher in the intervention arm although they were statistically non significant. In the present study, PEEP levels

were almost similar in the control group and in the interventional arm which could have led to similar improvements in gas exchange, respiratory mechanics in both the arms. Dual control mode (PCV-VG) was also used commonly in both groups. Moreover, the patients in the intervention arm had more severe disease with lower pH and lower HCO_3 compared to the control group. These findings are in coherence with the EPVENT 2 trial results.

Gattinoni et al. showed that secondary ARDS has increased chest wall elastance which might benefit for transpulmonary pressure guided PEEP.[63] Whereas the study population in the present study group had a higher incidence of severe ARDS with 68% of control and 78% of interventional group having severe ARDS. 56% of the present study population also had COVID -19 ARDS pneumonia. The presence of variable phenotypes of COVID-19 (L and H) which have different lung compliance and respond to PEEP differently might have also affected the study outcome Also, our results could be affected by the high number of patients with pulmonary embolism with COVID-19 pneumonia where ventilation strategy could not make much difference in oxygenation status.[64,65]

Fewer patients in the interventional group had VILI like pneumothorax and pneumomediastinum compared to the control group but it was not statistically significant (p-value 0.948). In EPVENT 2 trial, interventional group (5%) also had lower VILI events compared to the control group (6%) but was not statistically significant (p-value >0.99). The incidence of pneumothorax 12% and 8% in the control and interventional group, respectively, in the current study was higher as compared to EPVENT 2 trial because of the higher reported incidence of pneumothorax in COVID-19.[66] Use of high PEEP in L phenotype of COVID 19 might have led to a higher incidence of pneumothorax.

LIMITATIONS:

1. This was a single centre study with small sample size.
2. The most common etiology in our study population was COVID - 19 which affected ventilatory management due to the high incidence of pulmonary embolism in moderate to severe disease.[64]
3. Causative etiology was not classified into primary and secondary insults.
4. This trial enrolled a heterogeneous cohort of patients with moderate to severe ARDS including C-ARDS who have been shown to have high and low elastances.[65]
5. PES measurements are only obtained at a single point in the mid-esophagus and therefore may be insensitive to regional heterogeneity in pleural pressure.
6. Differences in Baseline ventilatory parameters were statistically significant but clinically non significant.
7. Intervention treatment applied only for 12 hours compared to 3 days in EPVENT 1 and 28 days in EPVENT 2 but VILI events were followed for up to 7 days.

SUMMARY & CONCLUSION

We conducted an institutional and prospective study in a tertiary care hospital for a duration of 1 year from April 2020 to April 2021. We enrolled 100 patients of moderate to severe ARDS Patients into two groups. One group received transpulmonary pressure guided ventilation while the other received conventional ventilation.

SALIENT FINDINGS:

- Transpulmonary pressure guided ventilation lead to a slight improvement in PaO2/FiO_2, and a/A ratios in the intervention group but they were not statistically significant.
- On further analysis, it was also found that Transpulmonary pressure guided ventilation lead to lower driving pressures compared to airway driving pressures which were statistically significant.
- Incidence of VILI in Transpulmonary pressure guided ventilation was low although statistically not significant.
- Transpulmonary pressure guided ventilation lead to improvement in CO_2 exchange in the intervention group which was statistically significant.

CONCLUSION:

Transpulmonary pressure guided ventilation lead to slight improvement in PaO_2/FiO_2, a/A ratios and CO_2 exchange clinically. Improvement in CO_2 exchange gained significance statistically also. VILI was also lower in the intervention arm as compared to the control arm.

RECOMMENDATIONS:

1. We recommend a transpulmonary pressure guided ventilation strategy for reduction in driving pressures and improvement of CO_2 exchange.
2. A large scale study which is adequately powered to detect changes in oxygenation and VILI in which both the groups are followed for a longer duration and esophageal pressures are also monitored in the conventional group.

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KEYS TO MASTER CHART

M	:	Male
F	:	Female
PCV-VG	:	Pressure Control Ventilation Volume Guaranteed
FiO2	:	Fraction of Inhaled Oxygen
TV	:	Tidal Volume
Rate	:	Respiratory Rate
PEEP	:	Positive End Expiratory Pressure
Ti	:	Inspiratory Time
PIP	:	Peak Inspiratory Pressure
PPLAT	:	Plateau Pressure
MAP	:	Mean Airway Pressure
DP	:	Driving Pressure
Comp(b)	:	Baseline Respiratory System Compliance
PES (end-expiratory hold)	:	Esophageal Pressure at End-Expiratory Hold
PTP (end-expiratory hold)	:	Transpulmonary Pressure at End-Expiratory Hold
Pes (end-inspiratory hold)	:	Esophageal Pressure at End-Inspiratory Hold
PTP (end-inspiratory hold)	:	Transpulmonary Pressure at End-Inspiratory Hold
tp DP	:	Transpulmonary Driving Pressure
pAO_2	:	partial pressure of Alveolar oxygen
pH	:	pH of arterial blood
paO2	:	partial pressure of arterial oxygen in mm. of Hg

paCO2	:	partial pressure of arterial carbon dioxide in mm. of Hg
hco3	:	concentration of HCO_3 in mEq/l
A-a	:	alveolar-arterial oxygen gradient
a/A	:	alveolar and arterial oxygen ratio
vili	:	ventilator-induced lung injury
PM	:	pneumomediastinum
Ptx	:	pneumothorax

Sr. No	MRD No.	Age	sex	sedative dose	NMB dose (ATRACURIUM)	MODE	VENTILATOR PARAMETERS (BASELINE)																
							FIO2	TV	rate	PEEP	Ti	PEAK	PPLAT	MAP	DP	cstat (b)	PES (end-expiratory hold)	PTP (end-expiratory hold)	Pes (end-inspiratory hold)	PTP (end-inspiratory hold)	tp DP	FIO2	TV	rate
1	1068372	86	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	22	12	0.9	40	32	28	20	21.25	N.A.	N.A.	N.A.	N.A.	N.A.	0.9	400	22
2	1033605	66	F	FENTANYL 70MCG/HR	30 MG/HR	PCV-VG	1	400	20	10	1	42	30	29	20	20.00	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	20
3	1027430	47	F	FENTANYL 60MCG/HR	50 MG/HR	PCV-VG	1	400	24	10	0.8	50	30	28	20	20.00	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24
4	1036419	22	M	FENTANYL 100MCG/HR	30 MG/HR	PCV-VG	1	400	20	8	1	28	26	22	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	22
5	1073150	61	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	22	12	0.9	42	28	26	16	25.00	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	22
6	1031438	38	M	FENTANYL 100MCG/HR	40 MG/HR	PCV-VG	0.8	400	22	12	0.9	32	28	24	16	25.00	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22
7	1067378	54	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	22	12	0.9	40	32	28	20	21.25	N.A.	N.A.	N.A.	N.A.	N.A.	0.9	400	22
8	1033104	60	F	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	20	10	1	42	30	29	20	20.00	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	20
9	1073138	61	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	22	12	0.9	42	29	25	17	23.53	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	22
10	1033524	49	M	FENTANYL 100MCG/HR	50 MG/HR	PCV-VG	1	425	20	10	1	38	30	25	20	21.25	N.A.	N.A.	N.A.	N.A.	N.A.	1	450	22
11	1087145	52	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	22	10	0.9	42	31	30	21	20.24	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24
12	1033438	38	M	FENTANYL 100MCG/HR	50 MG/HR	PCV-VG	0.8	400	22	12	0.9	32	28	24	16	25.00	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22
13	1032157	55	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	22	10	0.9	45	30	29	20	21.25	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24
14	1032152	55	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	22	10	0.9	45	30	28	20	21.25	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24
15	1068338	80	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	22	12	0.9	40	32	28	20	21.25	N.A.	N.A.	N.A.	N.A.	N.A.	0.9	400	22
16	1033689	44	F	FENTANYL 100MCG/HR	50 MG/HR	PCV-VG	1	400	20	10	1	42	30	26	20	20.00	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	20
17	1027734	47	F	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	1	400	24	10	0.8	45	30	24	20	20.00	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24
18	1036229	22	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	20	8	1	28	24	22	16	25.00	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	22
19	1073142	61	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	22	12	0.9	42	29	27	17	23.53	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	22
20	1035118	38	M	FENTANYL 100MCG/HR	50 MG/HR	PCV-VG	0.8	400	22	12	0.9	32	28	24	16	25.00	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22
21	1032254	55	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	22	10	0.9	45	30	26	20	21.25	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24
22	1068118	57	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	22	12	0.9	40	32	28	20	21.25	N.A.	N.A.	N.A.	N.A.	N.A.	0.9	400	22
23	1033629	66	F	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	20	10	1	42	30	29	20	20.00	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	20
24	1073056	61	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	22	12	0.9	42	29	27	17	23.53	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	22
25	10351438	38	M	FENTANYL 100MCG/HR	50 MG/HR	PCV-VG	0.8	400	22	12	0.9	32	30	24	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22
26	1032121	55	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	22	10	0.9	45	31	26	21	20.24	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24
27	1068568	28	M	FENTANYL 100MCG/HR	50 MG/HR	PCV-VG	1	425	22	12	0.9	40	30	28	18	23.61	N.A.	N.A.	N.A.	N.A.	N.A.	0.9	400	22
28	1032155	34	M	FENTANYL 100MCG/HR	50 MG/HR	PCV-VG	1	425	22	10	0.9	45	29	25	19	22.37	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24
29	1068345	72	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	22	12	0.9	40	30	28	18	23.61	N.A.	N.A.	N.A.	N.A.	N.A.	0.9	400	22
30	1033659	54	F	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	20	10	1	42	31	28	21	19.05	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	20
31	1023730	47	F	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	1	400	24	10	0.8	36	29	25	19	21.05	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24
32	1036421	22	M	FENTANYL 100MCG/HR	50 MG/HR	PCV-VG	1	400	20	8	1	28	24	22	16	25.00	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	22
33	1074356	61	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	22	12	0.9	42	30	26	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	22
34	1035478	38	M	FENTANYL 100MCG/HR	50 MG/HR	PCV-VG	0.8	400	22	12	0.9	32	28	24	16	25.00	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22
35	1032425	55	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	22	10	0.9	45	29	24	19	22.37	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24
36	1068343	37	M	FENTANYL 100MCG/HR	50 MG/HR	PCV-VG	1	425	22	12	0.9	40	31	28	19	22.37	N.A.	N.A.	N.A.	N.A.	N.A.	0.9	400	22
37	1033609	71	F	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	20	10	1	42	30	27	20	20.00	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	20
38	1071156	61	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	22	12	0.9	42	30	28	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	22
39	1035418	38	M	FENTANYL 100MCG/HR	50 MG/HR	PCV-VG	0.8	400	22	12	0.9	32	28	24	16	25.00	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22
40	1032225	55	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	22	10	0.9	45	32	30	22	19.32	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24
41	1068378	52	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	22	12	0.9	40	30	28	18	23.61	N.A.	N.A.	N.A.	N.A.	N.A.	0.9	400	22
42	1027730	47	F	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	1	400	24	10	0.8	47	31	25	21	19.05	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24
43	1033429	22	M	FENTANYL 100MCG/HR	50 MG/HR	PCV-VG	1	400	20	8	1	40	28	22	20	20.00	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	22
44	1073156	61	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	22	12	0.9	42	29	35	17	23.53	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	22
45	1014381	38	M	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	0.8	400	22	12	0.9	32	30	24	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22
46	1032125	55	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	22	10	0.9	45	30	27	20	21.25	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24
47	103214	66	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	22	10	0.9	45	29	26	19	22.37	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24
48	1035619	51	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	0.9	400	22	10	0.9	42	30	26	20	20.00	N.A.	N.A.	N.A.	N.A.	N.A.	0.9	400	22
49	1035438	38	M	FENTANYL 100MCG/HR	50 MG/HR	PCV-VG	0.8	400	22	12	0.9	32	28	24	16	25.00	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22
50	1073158	61	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	22	12	0.9	42	30	24	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	22

Sr. No	MRD No.	VENTILATOR PARAMETERS (@ 6 HOURS)												VENTILATOR PARAMETERS (@ 12 HOURS)												
		PEEP	Ti	PEAK	PPLAT	MAP	DP	cstat	PES (end-expiratory hold)	PTP (end-expiratory hold)	Pes (end-inspiratory hold)	PTP (end-inspiratory hold)	tp DP	FIO2	TV	rate	PEEP	Ti	PEAK	PPLAT	MAP	DP	CSTAT(E)	PES (end-expiratory hold)	PTP (end-expiratory hold)	Pes (end-inspiratory hold)
1	1068372	14	0.91	36	30	28	16	25	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	36	32	28	18	22.22	N.A.	N.A.	N.A.
2	1033605	12	1.00	43	31	28	19	21.05	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	20	12	1.00	43	30	28	18	22.22	N.A.	N.A.	N.A.
3	1027430	10	0.83	44	30	26	20	20	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	14	0.83	54	30	28	16	25.00	N.A.	N.A.	N.A.
4	1036419	10	0.91	30	26	19	16	25	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	30	26	19	12	33.33	N.A.	N.A.	N.A.
5	1073150	14	0.91	42	30	27	16	25	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	14	0.83	42	28	25	14	28.57	N.A.	N.A.	N.A.
6	1031438	14	0.91	34	29	24	15	26.67	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	34	28	18	14	28.57	N.A.	N.A.	N.A.
7	1067378	14	0.91	36	30	26	16	25	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	36	32	28	18	22.22	N.A.	N.A.	N.A.
8	1033104	12	1.00	43	30	25	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	20	12	1.00	43	30	28	18	22.22	N.A.	N.A.	N.A.
9	1073138	14	0.91	42	28	24	14	28.57	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	14	0.83	42	29	27	15	26.67	N.A.	N.A.	N.A.
10	1033524	10	0.91	39	30	26	20	22.5	N.A.	N.A.	N.A.	N.A.	N.A.	1	450	24	10	0.83	39	30	26	20	22.50	N.A.	N.A.	N.A.
11	1087145	12	0.83	42	30	23	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	12	0.83	46	30	25	18	22.22	N.A.	N.A.	N.A.
12	1033438	14	0.91	34	29	22	15	26.67	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	34	27	24	13	30.77	N.A.	N.A.	N.A.
13	1032157	12	0.83	42	30	25	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	12	0.83	40	30	25	18	22.22	N.A.	N.A.	N.A.
14	1032152	12	0.83	42	30	25	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	12	0.83	40	27	25	15	26.67	N.A.	N.A.	N.A.
15	1068338	14	0.91	36	30	28	16	25	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	36	32	28	18	22.22	N.A.	N.A.	N.A.
16	1033689	12	1.00	43	30	27	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	20	12	1.00	43	30	28	18	22.22	N.A.	N.A.	N.A.
17	1027734	10	0.83	41	30	25	20	20	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	14	0.83	54	30	28	16	25.00	N.A.	N.A.	N.A.
18	1036229	10	0.91	30	26	19	16	25	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	30	24	19	10	40.00	N.A.	N.A.	N.A.
19	1073142	14	0.91	42	30	24	16	25	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	14	0.83	42	29	23	15	26.67	N.A.	N.A.	N.A.
20	1035118	14	0.91	34	29	23	15	26.67	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	34	28	18	14	28.57	N.A.	N.A.	N.A.
21	1032254	12	0.83	42	30	25	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	12	0.83	40	30	25	18	22.22	N.A.	N.A.	N.A.
22	1068118	14	0.91	36	30	28	16	25	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	36	32	28	18	22.22	N.A.	N.A.	N.A.
23	1033629	12	1.00	43	30	28	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	20	12	1.00	43	30	28	18	22.22	N.A.	N.A.	N.A.
24	1073056	14	0.91	42	30	24	16	25	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	14	0.83	42	28	24	14	28.57	N.A.	N.A.	N.A.
25	10351438	14	0.91	34	29	22	15	26.67	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	34	27	18	13	30.77	N.A.	N.A.	N.A.
26	1032121	12	0.83	42	30	25	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	12	0.83	40	27	25	15	26.67	N.A.	N.A.	N.A.
27	1068568	14	0.91	36	30	28	16	25	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	36	30	28	16	25.00	N.A.	N.A.	N.A.
28	1032155	12	0.83	42	30	25	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	12	0.83	40	29	25	17	23.53	N.A.	N.A.	N.A.
29	1068345	14	0.91	36	30	28	16	25	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	36	30	28	16	25.00	N.A.	N.A.	N.A.
30	1033659	12	1.00	43	29	25	17	23.53	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	20	12	1.00	43	31	28	19	21.05	N.A.	N.A.	N.A.
31	1023730	10	0.83	42	30	26	20	20	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	14	0.83	54	29	28	15	26.67	N.A.	N.A.	N.A.
32	1036421	10	0.91	30	26	19	16	25	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	30	24	19	10	40.00	N.A.	N.A.	N.A.
33	1074356	14	0.91	42	30	24	16	25	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	14	0.83	42	30	25	16	25.00	N.A.	N.A.	N.A.
34	1035478	14	0.91	34	29	22	15	26.67	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	34	24	18	10	40.00	N.A.	N.A.	N.A.
35	1032425	12	0.83	42	30	25	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	12	0.83	40	29	25	17	23.53	N.A.	N.A.	N.A.
36	1068343	14	0.91	36	30	28	16	25	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	36	31	28	17	23.53	N.A.	N.A.	N.A.
37	1033609	12	1.00	43	30	24	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	20	12	1.00	43	30	28	18	22.22	N.A.	N.A.	N.A.
38	1071156	14	0.91	42	27	24	13	30.77	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	14	0.83	42	30	28	16	25.00	N.A.	N.A.	N.A.
39	1035418	14	0.91	34	29	22	15	26.67	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	34	28	18	14	28.57	N.A.	N.A.	N.A.
40	1032225	12	0.83	42	30	25	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	12	0.83	40	27	25	15	26.67	N.A.	N.A.	N.A.
41	1068378	14	0.91	36	30	28	16	25	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	36	30	28	16	25.00	N.A.	N.A.	N.A.
42	1027730	10	0.83	44	30	26	20	20	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	14	0.83	54	31	28	17	23.53	N.A.	N.A.	N.A.
43	1033429	10	0.91	30	26	22	16	25	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	30	26	22	12	33.33	N.A.	N.A.	N.A.
44	1073156	14	0.91	42	30	26	16	25	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	14	0.83	42	29	25	15	26.67	N.A.	N.A.	N.A.
45	1014381	14	0.91	34	29	24	15	26.67	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	34	30	18	16	25.00	N.A.	N.A.	N.A.
46	1032125	12	0.83	42	30	25	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	12	0.83	40	30	25	18	22.22	N.A.	N.A.	N.A.
47	103214	12	0.83	42	30	25	18	22.22	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	12	0.83	40	29	25	17	23.53	N.A.	N.A.	N.A.
48	1035619	12	0.91	44	35	27	23	17.39	N.A.	N.A.	N.A.	N.A.	N.A.	0.9	400	22	12	0.91	44	30	28	18	22.22	N.A.	N.A.	N.A.
49	1035438	14	0.91	34	29	24	15	26.67	N.A.	N.A.	N.A.	N.A.	N.A.	0.8	400	22	14	0.91	34	28	18	14	28.57	N.A.	N.A.	N.A.
50	1073158	14	0.91	42	30	25	16	25	N.A.	N.A.	N.A.	N.A.	N.A.	1	400	24	14	0.83	42	30	26	16	25.00	N.A.	N.A.	N.A.

Sr. No	MRD No.			baseline abg								abg at 6hrs					abg at 12 hrs							VILI
		PTP (end-inspiratory hold)	tp DP	pAo2	ph	pao2	pco2	hco3	paO2/fio2	A-a	a/A	ph	pao2	pco2	hco3	pAo2	ph	pao2	pco2	hco3	paO2/fio2	A-a	a/A	
1	1068372	N.A.	N.A.	663	7.26	123	40	19.2	123	540	0.19	7.22	85	49	20.1	521.65	7.48	125	39	20.1	156.25	396.65	0.24	PM
2	1033605	N.A.	N.A.	663	7.4	55	40	24	55	608	0.08	7.4	60	40	25	663	7.4	62	40	25.6	62	601	0.09	-
3	1027430	N.A.	N.A.	652	7.43	77	49	30.7	77	575	0.12	7.37	70	56	32.4	639.25	7.35	78	59	32.6	78	561.25	0.12	PTX
4	1036419	N.A.	N.A.	661	7.21	58	42	16.8	58	603	0.09	7.21	93	30	12	525.4	7.3	136	36	17.7	170	389.4	0.26	-
5	1073150	N.A.	N.A.	617	7.2	32	77	30	32	585	0.05	7.05	35	71	25.2	615.5	7.05	39	78	24	39	576.5	0.06	PTX,PM
6	1031438	N.A.	18	509.4	7.33	63	49	32.5	78.75	446.4	0.12	7.44	74	49	33.3	502.9	7.39	76	54	32.7	95	426.9	0.15	-
7	1067378	N.A.	13	663	7.26	119	40	19.2	119	544	0.18	7.22	85	49	20.1	521.65	7.48	96	39	20.1	120	425.65	0.18	PM
8	1033104	N.A.	10	663	7.4	57	40	24	57	606	0.09	7.4	60	40	25	663	7.4	62	40	25.6	62	601	0.09	-
9	1073138	N.A.	15	617	7.2	39	77	30	39	578	0.06	7.05	35	71	25.2	615.5	7.05	39	78	24	39	576.5	0.06	PTX
10	1033524	N.A.	13	640	7.24	87	59	25.3	87	553	0.14	7.21	84	59	21.3	661.75	7.33	91	41	21.6	91	570.75	0.14	-
11	1087145	N.A.	17	670	7.42	45	35	22.7	45	625	0.07	7.33	49	37	17.9	669.25	7.3	49	35	16	49	620.25	0.07	PM
12	1033438	N.A.	19	509.4	7.33	66	49	32.5	82.5	443.4	0.13	7.44	74	49	33.3	502.9	7.39	76	54	32.7	95	426.9	0.15	-
13	1032157	N.A.	14	670	7.16	103	35	12.5	103	567	0.15	7.2	100	35	14	675.5	7.25	108	30	14	108	567.5	0.16	-
14	1032152	N.A.	14	670	7.16	102	35	12.5	102	568	0.15	7.2	100	35	14	675.5	7.25	110	30	14	110	565.5	0.16	-
15	1068338	N.A.	16	663	7.26	116	40	19.2	116	547	0.17	7.22	85	49	20.1	521.65	7.48	100	39	20.1	125	421.65	0.19	-
16	1033689	N.A.	14	663	7.4	59	40	24	59	604	0.09	7.4	60	40	25	663	7.4	62	40	25.6	62	601	0.09	-
17	1027734	N.A.	20	652	7.43	78	49	30.7	78	574	0.12	7.37	70	56	32.4	639.25	7.35	60	59	32.6	60	579.25	0.09	-
18	1036229	N.A.	13	661	7.21	61	42	16.8	61	600	0.09	7.21	93	30	12	525.4	7.3	132	36	17.7	165	393.4	0.25	PTX
19	1073142	N.A.	17	617	7.2	38	77	30	38	579	0.06	7.05	35	71	25.2	615.5	7.05	39	78	24	39	576.5	0.06	PM
20	1035118	N.A.	19	509.4	7.33	69	49	32.5	86.25	440.4	0.14	7.44	74	49	33.3	502.9	7.39	76	54	32.7	95	426.9	0.15	-
21	1032254	N.A.	14	670	7.16	108	35	12.5	108	562	0.16	7.2	100	35	14	675.5	7.25	108	30	14	108	567.5	0.16	-
22	1068118	N.A.	14	663	7.26	105	40	19.2	105	558	0.16	7.22	85	49	20.1	521.65	7.4	85	39	20.1	106.25	436.65	0.16	PM
23	1033629	N.A.	16	663	7.4	52	40	24	52	611	0.08	7.4	60	40	25	663	7.4	62	40	25.6	62	601	0.09	-
24	1073056	N.A.	14	617	7.2	39	77	30	39	578	0.06	7.05	35	71	25.2	615.5	7.05	39	78	24	39	576.5	0.06	PM
25	10351438	N.A.	20	509.4	7.33	72	49	32.5	90	437.4	0.14	7.44	74	49	33.3	502.9	7.39	76	54	32.7	95	426.9	0.15	-
26	1032121	N.A.	13	670	7.16	100	35	12.5	100	570	0.15	7.2	100	35	14	675.5	7.25	108	30	14	108	567.5	0.16	-
27	1068568	N.A.	14	663	7.26	104	40	19.2	104	559	0.16	7.22	85	49	20.1	521.65	7.42	102	39	20.1	127.5	419.65	0.20	PM
28	1032155	N.A.	20	670	7.16	107	35	12.5	107	563	0.16	7.2	100	35	14	675.5	7.25	106	30	14	106	569.5	0.16	-
29	1068345	N.A.	13	663	7.26	110	40	19.2	110	553	0.17	7.22	85	49	20.1	521.65	7.42	88	39	20.1	110	433.65	0.17	PM
30	1033659	N.A.	17	663	7.4	53	40	24	53	610	0.08	7.4	60	40	25	663	7.4	65	40	25.6	65	598	0.10	-
31	1023730	N.A.	19	652	7.43	78	49	30.7	78	574	0.12	7.37	70	56	32.4	639.25	7.35	64	59	32.6	64	575.25	0.10	-
32	1036421	N.A.	14	661	7.21	65	42	16.8	65	596	0.10	7.21	93	30	12	525.4	7.3	120	36	17.7	150	405.4	0.23	PTX
33	1074356	N.A.	10	617	7.2	30	77	30	30	587	0.05	7.05	35	71	25.2	615.5	7.05	39	78	24	39	576.5	0.06	PM,PTX
34	1035478	N.A.	15	509.4	7.33	64	49	32.5	80	445.4	0.13	7.44	74	49	33.3	502.9	7.39	76	54	32.7	95	426.9	0.15	-
35	1032425	N.A.	13	670	7.16	110	35	12.5	110	560	0.16	7.2	100	35	14	675.5	7.25	108	30	14	108	567.5	0.16	-
36	1068343	N.A.	17	663	7.26	101	40	19.2	101	562	0.15	7.22	85	49	20.1	521.65	7.48	97	39	20.1	121.25	424.65	0.19	PM
37	1033609	N.A.	19	663	7.4	54	40	24	54	609	0.08	7.4	60	40	25	663	7.4	69	40	25.6	69	594	0.10	-
38	1071156	N.A.	14	617	7.2	31	77	30	31	586	0.05	7.05	35	71	25.2	615.5	7.05	42	78	24	42	573.5	0.07	PM
39	1035418	N.A.	14	509.4	7.33	64	49	32.5	80	445.4	0.13	7.44	74	49	33.3	502.9	7.39	76	54	32.7	95	426.9	0.15	-
40	1032225	N.A.	16	670	7.16	109	35	12.5	109	561	0.16	7.2	100	35	14	675.5	7.25	108	30	14	108	567.5	0.16	-
41	1068378	N.A.	14	663	7.26	112	40	19.2	112	551	0.17	7.22	85	49	20.1	521.65	7.48	92	39	20.1	115	429.65	0.18	PM
42	1027730	N.A.	20	652	7.43	76	49	30.7	76	576	0.12	7.37	70	56	32.4	639.25	7.35	61	59	32.6	61	578.25	0.10	-
43	1033429	N.A.	13	661	7.21	60	42	16.8	60	601	0.09	7.21	93	30	12	525.4	7.3	144	36	17.7	180	381.4	0.27	-
44	1073156	N.A.	20	617	7.2	31	77	30	31	586	0.05	7.05	35	71	25.2	615.5	7.05	46	78	24	46	569.5	0.07	PTX
45	1014381	N.A.	13	509.4	7.33	64	49	32.5	80	445.4	0.13	7.44	74	49	33.3	502.9	7.39	75	54	32.7	93.75	427.9	0.15	-
46	1032125	N.A.	14	670	7.16	106	35	12.5	106	564	0.16	7.2	100	35	14	675.5	7.25	110	30	14	110	565.5	0.16	-
47	103214	N.A.	20	670	7.16	113	35	12.5	113	557	0.17	7.2	100	35	14	675.5	7.25	102	30	14	102	573.5	0.15	-
48	1035619	N.A.	13	573.7	7.32	74	55	24	82.22	499.7	0.13	7.34	68	52	24	576.7	7.34	68	52	25	75.56	508.7	0.12	PTX
49	1035438	N.A.	17	509.4	7.33	75	49	32.5	93.75	434.4	0.15	7.44	74	49	33.3	502.9	7.39	76	54	32.7	95	426.9	0.15	-
50	1073158	N.A.	19	617	7.2	42	77	30	42	575	0.07	7.05	35	71	25.2	615.5	7.05	56	78	24	56	559.5	0.09	PM

Sr. No	M.R.D.	Age	sex	sedative dose	NMB dose (ATRACURIUM)	MODE	VENTILATOR PARAMETERS (BASELINE)																	
							FIO2	TV	rate	PEEP	Ti	PEAK	PPLAT	MAP	DP	cstat (b)	PES (end-expiratory hold)	PTP (end-expiratory hold)	Pes (end-inspiratory hold)	PTP (end-inspiratory hold)	tp DP	FIO2	TV	rate
1	1068378	42	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	16	12	1.3	38	32	16	20	21.25	8	10	27	30	20	1	400	24
2	1073269	53	F	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	24	12	0.83	35	31	28	19	21.05	4	10	15	24	14	1	400	24
3	1088707	40	F	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	0.5	450	20	10	1	32	27	18	17	26.47	3	9	13	19	10	0.5	450	20
4	502500	60	f	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	0.8	450	18	12	1.11	31	28	18	16	28.13	4	9	14	24	15	0.8	450	20
5	671661	58	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	0.8	450	18	12	1.11	32	22	17	10	45.00	5	11	14	22	11	0.8	450	20
6	1042411	62	M	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	1	425	22	12	0.91	38	34	22	22	19.32	8	12	22	26	14	1	425	22
7	1037493	50	m	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	0.9	425	20	18	1	44	35	26	17	25.00	6	12	18	34	22	0.9	425	20
8	1086050	42	f	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	0.5	425	16	8	1.3	24	22	14	14	30.36	3	8	12	18	10	0.6	425	16
9	1041155	48	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	450	20	12	1	28	24	16	12	37.50	5	11	18	25	14	1	450	20
10	548492	71	m	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	22	12	0.91	44	35	27	23	18.48	8	12	22	26	14	1	425	22
11	1073338	41	f	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	450	26	12	0.77	33	24	18	12	37.50	5	10	15	22	12	1	450	26
12	1049129	43	M	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	1	425	22	10	0.91	41	30	23	20	21.25	6	12	15	32	20	1	450	24
13	1049129	38	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	22	14	0.91	40	32	24	18	22.22	4	10	14	22	12	1	400	22
14	1042411	76	f	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	1	425	22	12	0.91	38	34	22	22	19.32	8	12	22	26	14	1	425	22
15	1037493	57	m	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	0.9	425	20	16	1	44	35	19	19	22.37	6	12	18	34	22	0.9	425	20
16	1086050	59	f	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	0.5	425	16	8	1.3	27	22	14	14	30.36	3	8	12	18	10	0.6	425	16
17	1041155	44	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	450	20	12	1	28	24	16	12	37.50	5	11	18	25	14	1	450	20
18	548492	29	m	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	22	12	0.91	44	35	27	23	18.48	8	12	22	26	14	1	425	22
19	1073338	36	f	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	450	26	12	0.77	33	24	18	12	37.50	5	10	15	22	12	1	450	26
20	1049129	68	M	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	1	425	22	10	0.91	41	30	23	20	21.25	6	12	15	32	20	1	450	24
21	1049129	48	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	22	14	0.91	40	32	24	18	22.22	4	10	14	22	12	1	400	22
22	1073338	70	f	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	450	26	12	0.77	33	24	18	12	37.50	5	10	15	22	12	1	450	26
23	1049129	69	M	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	1	425	22	14	0.91	41	30	23	16	26.56	6	12	15	32	20	1	450	24
24	1049129	67	f	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	22	14	0.91	40	32	24	18	22.22	4	10	14	22	12	1	400	22
25	1042411	46	M	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	1	425	22	14	0.91	38	34	22	20	21.25	8	12	22	26	14	1	425	22
26	1037493	37	f	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	0.9	425	20	16	1	44	35	19	19	22.37	6	12	18	34	22	0.9	425	20
27	1086050	28	f	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	0.5	425	16	8	1.3	24	22	14	14	30.36	3	8	12	18	10	0.6	425	16
28	1088707	47	F	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	0.5	450	20	10	1	32	27	18	17	26.47	3	9	13	19	10	0.5	450	20
29	502500	39	f	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	0.8	450	18	12	1.11	36	28	18	16	28.13	4	9	14	24	15	0.8	450	20
30	671661	58	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	0.8	450	18	12	1.11	32	22	17	10	45.00	5	11	14	22	11	0.8	450	20
31	1042411	32	M	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	1	425	22	12	0.91	38	34	22	22	19.32	8	12	22	26	14	1	425	22
32	1037493	74	f	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	0.9	425	20	16	1	44	35	19	19	22.37	6	12	18	34	22	0.9	425	20
33	1086050	79	f	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	0.5	425	16	8	1.3	24	22	11	14	30.36	3	8	12	18	10	0.6	425	16
34	1041155	80	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	450	20	12	1	28	24	16	12	37.50	5	11	18	25	14	1	450	20
35	548492	84	m	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	425	22	12	0.91	44	35	27	23	18.48	8	12	22	26	14	1	425	22
36	1073338	61	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	450	26	12	0.77	33	24	18	12	37.50	5	10	15	22	12	1	450	26
37	1049129	35	f	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	1	425	22	12	0.91	41	30	23	18	23.61	6	12	15	32	20	1	450	24
38	1049129	49	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	22	14	0.91	40	32	24	18	22.22	4	10	14	22	12	1	400	22
39	1049129	77	M	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	1	425	22	14	0.91	41	30	23	16	26.56	6	12	15	32	20	1	450	24
40	1049129	31	f	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	22	14	0.91	40	32	24	18	22.22	4	10	14	22	12	1	400	22
41	1073338	52	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	450	26	12	0.77	33	24	18	12	37.50	5	10	15	22	12	1	450	26
42	1049129	55	f	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	1	425	22	14	0.91	41	30	23	16	26.56	6	12	15	32	20	1	450	24
43	1049129	50	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	1	400	22	14	0.91	40	32	24	18	22.22	4	10	14	22	12	1	400	22
44	1042411	51	f	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	1	425	22	12	0.91	38	34	22	22	19.32	8	12	22	26	14	1	425	22
45	1037493	72	m	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	0.9	425	20	18	1	44	35	19	17	25.00	6	12	18	34	22	0.9	425	20
46	1086050	66	f	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	0.5	425	16	8	1.3	24	22	11	14	30.36	3	8	12	18	10	0.6	425	16
47	1088707	69	F	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	0.5	450	20	10	1	32	27	18	17	26.47	3	9	13	19	10	0.5	450	20
48	502500	64	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	0.8	450	18	12	1.11	31	28	18	16	28.13	4	9	14	24	15	0.8	450	20
49	671661	34	M	FENTANYL 80MCG/HR	30 MG/HR	PCV-VG	0.8	450	18	12	1.11	32	22	17	10	45.00	5	11	14	22	11	0.8	450	20
50	1042411	65	f	FENTANYL 80MCG/HR	40 MG/HR	PCV-VG	1	425	22	12	0.91	38	34	22	22	19.32	8	12	22	26	14	1	425	22

Sr. No	M.R.D.	VENTILATOR PARAMETERS (@ 6 HOURS)												VENTILATOR PARAMETERS (@ 12 HOURS)										
		PEEP	Ti	PEAK	PPLAT	MAP	DP	cstat	PES (end-expiratory hold)	PTP (end-expiratory hold)	Pes (end-inspiratory hold)	PTP (end-inspiratory hold)	tp DP	FIO2	TV	rate	PEEP	Ti	PEAK	PPLAT	MAP	DP	CSTAT(E)	PES (end-expiratory hold)
1	1068378	14	0.83	38	30	24	16	25	5	12	28	30	18	1	400	24	14	0.83	38	30	25	16	25	5
2	1073269	12	0.83	45	31	28	19	21.05	4	10	15	24	14	1	400	26	12	0.77	45	31	24	19	21.05	4
3	1088707	8	1.00	32	27	18	19	23.68	8	3	13	19	16	0.5	450	18	10	1.11	34	27	18	17	26.47	3
4	502500	12	1.00	33	29	19	17	26.47	4	9	14	24	15	0.8	450	20	14	1.00	34	30	19	16	28.13	6
5	671661	12	1.00	32	22	17	10	45	5	11	14	22	11	0.8	450	24	12	0.83	34	22	17	10	45	5
6	1042411	12	0.91	39	34	22	22	19.32	8	12	22	26	14	1	425	22	14	0.91	40	35	26	21	20.24	7
7	1037493	10	1.00	45	35	20	25	17	6	10	18	32	22	0.9	425	20	12	1.00	45	35	24	23	18.48	7
8	1086050	10	1.25	27	24	20	14	30.36	3	8	16	22	14	0.6	425	16	10	1.25	26	24	20	14	30.36	3
9	1041155	12	1.00	32	26	20	14	32.14	5	11	18	25	14	0.9	450	20	12	1.00	32	26	20	14	32.14	5
10	548492	12	0.91	45	35	27	23	18.48	8	12	22	26	14	1	425	22	14	0.91	45	35	28	21	20.24	7
11	1073338	12	0.77	33	26	18	14	32.14	5	10	15	22	12	1	450	26	14	0.77	36	28	23	14	32.14	5
12	1049129	12	0.83	42	30	23	18	25	6	12	16	30	18	1	450	26	12	0.77	42	31	24	19	23.68	6
13	1049129	14	0.91	40	32	24	18	22.22	5	10	15	22	12	1	400	26	16	0.77	42	34	25	18	22.22	5
14	1042411	12	0.91	39	34	22	22	19.32	8	12	22	26	14	1	425	22	14	0.91	40	35	26	21	20.24	7
15	1037493	10	1.00	45	35	20	25	17	6	10	18	32	22	0.9	425	20	12	1.00	45	35	24	23	18.48	7
16	1086050	10	1.25	27	24	20	14	30.36	3	8	16	22	14	0.6	425	16	10	1.25	26	24	20	14	30.36	3
17	1041155	12	1.00	32	26	20	14	32.14	5	11	18	25	14	0.9	450	20	12	1.00	32	26	20	14	32.14	5
18	548492	12	0.91	45	35	27	23	18.48	8	12	22	26	14	1	425	22	14	0.91	45	35	28	21	20.24	7
19	1073338	12	0.77	33	26	18	14	32.14	5	10	15	22	12	1	450	26	14	0.77	36	28	23	14	32.14	5
20	1049129	14	0.83	42	30	23	16	28.13	6	12	16	30	18	1	450	26	12	0.77	42	31	24	19	23.68	6
21	1049129	14	0.91	40	32	24	18	22.22	5	10	15	22	12	1	400	26	16	0.77	42	34	25	18	22.22	5
22	1073338	12	0.77	33	26	18	14	32.14	5	10	15	22	12	1	450	26	14	0.77	36	28	23	14	32.14	5
23	1049129	12	0.83	42	30	23	18	25	6	12	16	30	18	1	450	26	12	0.77	42	31	24	19	23.68	6
24	1049129	14	0.91	40	32	24	18	22.22	5	10	15	22	12	1	400	26	16	0.77	42	34	25	18	22.22	5
25	1042411	12	0.91	39	34	22	22	19.32	8	12	22	26	14	1	425	22	14	0.91	40	35	26	21	20.24	7
26	1037493	10	1.00	45	35	20	25	17	6	10	18	32	22	0.9	425	20	12	1.00	45	35	24	23	18.48	7
27	1086050	10	1.25	27	24	20	14	30.36	3	8	16	22	14	0.6	425	16	10	1.25	26	24	20	14	30.36	3
28	1088707	8	1.00	32	27	18	19	23.68	8	3	13	19	16	0.5	450	18	10	1.11	34	27	18	17	26.47	3
29	502500	12	1.00	33	29	19	17	26.47	4	9	14	24	15	0.8	450	20	14	1.00	34	30	19	16	28.13	6
30	671661	12	1.00	32	22	17	10	45	5	11	14	22	11	0.8	450	24	12	0.83	34	22	17	10	45	5
31	1042411	12	0.91	39	34	22	22	19.32	8	12	22	26	14	1	425	22	14	0.91	40	35	26	21	20.24	7
32	1037493	10	1.00	45	35	20	25	17	6	10	18	32	22	0.9	425	20	12	1.00	45	35	24	23	18.48	7
33	1086050	10	1.25	27	24	20	14	30.36	3	8	16	22	14	0.6	425	16	10	1.25	26	24	20	14	30.36	3
34	1041155	12	1.00	32	26	20	14	32.14	5	11	18	25	14	0.9	450	20	12	1.00	32	26	20	14	32.14	5
35	548492	12	0.91	45	35	27	23	18.48	8	12	22	26	14	1	425	22	14	0.91	45	35	28	21	20.24	7
36	1073338	12	0.77	33	26	18	14	32.14	5	10	15	22	12	1	450	26	14	0.77	36	28	23	14	32.14	5
37	1049129	12	0.83	42	30	23	18	25	6	12	16	30	18	1	450	26	12	0.77	42	31	24	19	23.68	6
38	1049129	14	0.91	40	32	24	18	22.22	5	10	15	22	12	1	400	26	16	0.77	42	34	25	18	22.22	5
39	1049129	12	0.83	42	30	23	18	25.00	6	12	16	30	18	1	450	26	12	0.77	42	31	24	19	23.68	6
40	1049129	14	0.91	40	32	24	18	22.22	5	10	15	22	12	1	400	26	16	0.77	42	34	25	18	22.22	5
41	1073338	12	0.77	33	26	18	14	32.14	5	10	15	22	12	1	450	26	14	0.77	36	28	23	14	32.14	5
42	1049129	14	0.83	42	30	23	16	28.13	6	12	16	30	18	1	450	26	12	0.77	42	31	24	19	23.68	6
43	1049129	14	0.91	40	32	24	18	22.22	5	10	15	22	12	1	400	26	16	0.77	42	34	25	18	22.22	5
44	1042411	12	0.91	39	34	22	22	19.32	8	12	22	26	14	1	425	22	14	0.91	40	35	26	21	20.24	7
45	1037493	10	1.00	45	35	20	25	17.00	6	10	18	32	22	0.9	425	20	12	1.00	45	35	24	23	18.48	7
46	1086050	10	1.25	27	24	20	14	30.36	3	8	16	22	14	0.6	425	16	10	1.25	26	24	20	14	30.36	3
47	1088707	8	1.00	32	27	18	19	23.68	8	3	13	19	16	0.5	450	18	10	1.11	34	27	18	17	26.47	3
48	502500	12	1.00	33	29	19	17	26.47	4	9	14	24	15	0.8	450	20	14	1.00	34	30	19	16	28.13	6
49	671661	12	1.00	32	22	17	10	45.00	5	11	14	22	11	0.8	450	24	12	0.83	34	22	17	10	45	5
50	1042411	12	0.91	39	34	22	22	19.32	8	12	22	26	14	1	425	22	14	0.91	40	35	26	21	20.24	7

Sr. No	M.R.D.					baseline abg								abg at 6hrs					abg at 12 hrs							VILI
		PTP (end-expiratory hold)	Pes (end-inspiratory hold)	PTP (end-inspiratory hold)	tp DP	pAo2	ph	pao2	pco2	hco3	paO2/fio2	A-a	a/A	ph	pao2	pco2	hco3	pAo2	ph	pao2	pco2	hco3	paO2/fio2	A-a	a/A	
1	1068378	12	26	30	18	539.81	7.46	68	33	25.1	68	471.81	0.13	7.48	60	34	25	668	7.44	69	36	24	69.00	599.00	0.10	PM
2	1073269	11	17	24	13	607.92	6.8	73	77	14.1	73	534.92	0.12	7.38	92	39	23.1	664.25	7.4	97	39	23.4	97.00	567.25	0.15	-
3	1088707	9	13	19	10	574.88	7.48	100	27	20.1	200	474.88	0.17	7.43	101	26	17.3	319	7.43	110	30	17.3	220.00	209.00	0.34	-
4	502500	11	16	26	15	602.91	7.01	48	72	18	60	554.91	0.08	7.21	51	39	15.6	520.4	7.29	88	40	19.2	110.00	432.40	0.17	-
5	671661	11	16	24	13	584.95	7.2	106	52	20.3	132.5	478.95	0.18	7.2	103	50	19.5	507.9	7.2	104	50	19.5	130.00	403.90	0.20	-
6	1042411	10	24	27	17	446.28	7.22	61	50	20	61	385.28	0.14	7.21	80	50	20	648	7.19	83	52	18	83.00	565.00	0.13	-
7	1037493	11	18	30	19	543.82	7.43	74	47	31.9	82.22	469.82	0.14	7.4	76	44	31	586.7	7.4	81	44	31	90.00	505.70	0.14	-
8	1086050	8	16	22	14	605.91	7.48	54	33	25.1	108	551.91	0.09	7.48	60	34	25	382.8	7.44	61	36	24	101.67	321.80	0.16	PM
9	1041155	11	18	25	14	577.94	7.21	89	52	20.3	89	488.94	0.15	7.2	103	50	19.5	579.2	7.22	109	50	19.2	121.11	470.20	0.19	-
10	548492	11	24	27	16	552.86	7.23	79	50	20	79	473.86	0.14	7.21	80	50	20	648	7.19	84	52	19	84.00	564.00	0.13	-
11	1073338	11	18	25	14	624.93	7.46	42	36	28.1	42	582.93	0.07	7.5	49	34	28	665.5	7.45	55	38	26	55.00	610.50	0.08	PM,PTX
12	1049129	11	17	31	20	443.27	6.85	32	76	14	32	411.27	0.07	7	50	70	14	654.25	7.39	68	47	24.8	68.00	586.25	0.10	PM
13	1049129	12	18	25	13	566.85	6.89	39	74	10	39	527.85	0.07	7	54	63	12	624.25	6.9	67	71	10	67.00	557.25	0.11	PM
14	1042411	10	24	27	17	567.85	7.24	65	50	20	65	502.85	0.11	7.21	80	50	20	648	7.19	75	52	18	75.00	573.00	0.12	-
15	1037493	11	18	30	19	546.83	7.46	77	47	31.9	85.56	469.83	0.14	7.4	76	44	31	586.7	7.4	74	44	31	82.22	512.70	0.13	-
16	1086050	8	16	22	14	603.91	7.5	53	33	25.1	106	550.91	0.09	7.48	60	34	25	382.8	7.44	71	36	24	118.33	311.80	0.19	PM
17	1041155	11	18	25	14	573.88	7.18	84	52	20.3	84	489.88	0.15	7.2	103	50	19.5	579.2	7.22	70	50	19.2	77.78	509.20	0.12	-
18	548492	11	24	27	16	599.91	7.19	76	50	20	76	523.91	0.13	7.21	80	50	20	648	7.19	74	52	19	74.00	574.00	0.11	-
19	1073338	11	18	25	14	578.94	7.51	44	36	28.1	44	534.94	0.08	7.5	49	34	28	665.5	7.45	72	38	26	72.00	593.50	0.11	PM
20	1049129	11	17	31	20	440.26	6.9	38	76	14	38	402.26	0.09	7	50	70	14	656.75	7.39	60	45	24.8	60.00	596.75	0.09	PTX
21	1049129	12	18	25	13	561.84	6.9	49	74	10	49	512.84	0.09	7	54	63	12	625.5	6.9	59	70	10	59.00	566.50	0.09	PM
22	1073338	11	18	25	14	557.84	7.54	57	36	28.1	57	500.84	0.10	7.5	49	34	28	665.5	7.45	65	38	26	65.00	600.50	0.10	PM
23	1049129	11	17	31	20	610.92	6.9	35	76	14	35	575.92	0.06	7	50	70	14	653	7.39	53	48	24.8	53.00	600.00	0.08	PTX
24	1049129	12	18	25	13	577.94	6.92	41	74	10	41	536.94	0.07	7	54	63	12	628	6.9	51	68	10	51.00	577.00	0.08	-
25	1042411	10	24	27	17	437.26	7.26	62	50	20	62	375.26	0.14	7.21	80	50	20	648	7.19	86	52	18	86.00	562.00	0.13	PM
26	1037493	11	18	30	19	569.85	7.49	57	33	25.1	63.33	512.85	0.10	7.48	60	34	25	596.7	7.44	64	36	24	71.11	532.70	0.11	-
27	1086050	8	16	22	14	558.84	6.86	81	77	14.1	162	477.84	0.14	7.38	92	39	23.1	379.05	7.4	94	39	23.4	156.67	285.05	0.25	-
28	1088707	9	13	19	10	562.84	7.47	102	27	20.1	204	460.84	0.18	7.43	101	26	17.3	319	7.43	112	30	17.3	224.00	207.00	0.35	-
29	502500	11	16	26	15	552.83	7.02	50	72	18	62.5	502.83	0.09	7.21	51	39	15.6	520.4	7.29	79	40	19.2	98.75	441.40	0.15	-
30	671661	11	16	24	13	609.92	7.2	114	52	20.3	142.5	495.92	0.19	7.2	103	50	19.5	507.9	7.2	101	50	19.5	126.25	406.90	0.20	-
31	1042411	10	24	27	17	573.88	7.24	64	50	20	64	509.88	0.11	7.21	80	50	20	648	7.19	77	52	18	77.00	571.00	0.12	-
32	1037493	11	18	30	19	595.90	7.44	87	47	31.9	96.67	508.90	0.15	7.4	76	44	31	586.7	7.4	80	44	31	88.89	506.70	0.14	-
33	1086050	8	16	22	14	586.95	7.49	56	33	25.1	112	530.95	0.10	7.48	60	34	25	382.8	7.44	67	36	24	111.67	315.80	0.18	PTX
34	1041155	11	18	25	14	445.27	7.2	88	52	20.3	88	357.27	0.20	7.2	103	50	19.5	579.2	7.22	117	50	19.2	130.00	462.20	0.20	-
35	548492	11	24	27	16	559.84	7.21	71	50	20	71	488.84	0.13	7.21	80	50	20	648	7.19	89	52	19	89.00	559.00	0.14	-
36	1073338	11	18	25	14	561.85	7.5	49	36	28.1	49	512.85	0.09	7.5	49	34	28	665.5	7.45	64	38	26	64.00	601.50	0.10	-
37	1049129	11	17	31	20	608.92	6.9	37	76	14	37	571.92	0.06	7	50	70	14	656.75	7.39	63	45	24.8	63.00	593.75	0.10	-
38	1049129	12	18	25	13	585.95	6.92	50	74	10	50	535.95	0.09	7	54	63	12	625.5	6.9	62	70	10	62.00	563.50	0.10	-
39	1049129	11	17	31	20	445.27	6.9	56	76	14	56	389.27	0.13	7	50	70	14	656.75	7.39	64	45	24.8	64.00	592.75	0.10	-
40	1049129	12	18	25	13	560.84	6.9	40	74	10	40	520.84	0.07	7	54	63	12	625.5	6.9	67	70	10	67.00	558.50	0.11	-
41	1073338	11	18	25	14	550.83	7.5	51	36	28.1	51	499.83	0.09	7.5	49	34	28	665.5	7.45	60	38	26	60.00	605.50	0.09	-
42	1049129	11	17	31	20	575.88	6.9	36	76	14	36	539.88	0.06	7	50	70	14	656.75	7.39	66	45	24.8	66.00	590.75	0.10	-
43	1049129	12	18	25	13	600.91	6.9	47	74	10	47	553.91	0.08	7	54	63	12	623	6.9	54	72	10	54.00	569.00	0.09	PTX
44	1042411	10	24	27	17	585.95	7.21	72	50	20	72	513.95	0.12	7.21	80	50	20	648	7.19	71	52	19	71.00	577.00	0.11	-
45	1037493	11	18	30	19	445.27	7.49	55	33	25.1	61.11	390.27	0.12	7.48	60	34	25	596.7	7.44	62	36	24	68.89	534.70	0.10	-
46	1086050	8	16	22	14	563.84	6.87	78	77	14.1	156	485.84	0.14	7.38	92	39	23.1	379.05	7.4	98	39	23.4	163.33	281.05	0.26	-
47	1088707	9	13	19	10	556.83	7.48	99	27	20.1	198	457.83	0.18	7.43	101	26	17.3	319	7.43	108	30	17.3	216.00	211.00	0.34	-
48	502500	11	16	26	15	499.57	7.02	50	72	18	62.5	449.57	0.10	7.21	51	39	15.6	520.4	7.29	99	40	19.2	123.75	421.40	0.19	-
49	671661	11	16	24	13	434.25	7.2	109	52	20.3	136.25	325.25	0.25	7.2	103	50	19.5	507.9	7.2	106	50	19.5	132.50	401.90	0.21	-
50	1042411	10	24	27	17	574.93	7.23	60	50	20	60	514.93	0.10	7.21	80	50	20	648	7.19	85	52	18	85.00	563.00	0.13	-

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Date 2/9/2021

The Principal,
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Subject: Approval of Plan of Thesis.

This is to inform you that the Faculty of Medical Sciences in its meeting held on 22.01.2021 has approved the plan of thesis of Dr M Ravi Krishna, a student of your college for DM Critical Care Medicine along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
Comparative evaluation of transpulmonary pressure guided ventilation versus conventional ventilation in patients with ards

Supervisor
Dr. Parshotam Lal Gautam
Prof. & Head,
Dept. of Critical Care Medicine,
DMCH, Ludhiana.

Co-Supervisor
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The student has to submit the three copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*

COMPARATIVE EVALUATION OF TRANSPULMONARY PRESSURE GUIDED VENTILATION VERSUS CONVENTIONAL VENTILATION IN PATIENTS WITH ARDS

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

DOCTORATE OF MEDICINE

IN

CRITICAL CARE MEDICINE

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES
FARIDKOT

FEBRUARY, 2020

DR. M. RAVI KRISHNA

DEPARTMENT OF CRITICAL CARE MEDICINE
DAYANAND MEDICAL COLLEGE & HOSPITAL
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ABSTRACT OF PLAN OF THESIS

Title	COMPARATIVE EVALUATION OF TRANSPULMONARY PRESSURE GUIDED VENTILATION VERSUS CONVENTIONAL VENTILATION IN PATIENTS WITH ARDS
For the degree of	D.M. CRITICAL CARE MEDICINE
Name of the candidate	Dr. M. RAVI KRISHNA
Supervisor	Dr. Parshotam Lal Gautam, Professor & Head, Department of Critical Care Medicine, DMCH, Ludhiana
Co-supervisor	Dr. Gunchan Paul, Associate Professor, Department of Critical Care Medicine, DMCH, Ludhiana
Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: As per ARDS net study mechanical-ventilation strategies that use lower end-inspiratory (plateau) airway pressures, lower tidal volumes (VT), and higher positive end-expiratory pressures (PEEPs) can improve survival in patients with the acute respiratory distress syndrome (ARDS)1, but the optimal pressures are not known. Transpulmonary pressure guided ventilation may be beneficial in such patients without the drawback of conventional ventilation strategy.

Aim of Study: Our aim is to compare the effect of transpulmonary pressure guided ventilation versus conventional ventilation in patients with A.R.D.S.

Materials & Methods: A randomized prospective study will be conducted on 100 patients of moderate to severe ARDS Patients will be randomly allocated into two groups. Group T will receive transpulmonary pressure guided ventilation and Group C will receive conventional ventilation.

Clinical Significance: This study will help us to find out if transpulmonary pressure guided ventilation improves ventilation parameters.

Keywords: TRANSPULMONARY PRESSURE GUIDED VENTILATION, CONVENTIONAL VENTILATION STRATEGY.

(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"COMPARATIVE EVALUATION OF TRANSPULMONARY PRESSURE GUIDED VENTILATION VERSUS CONVENTIONAL VENTILATION IN PATIENTS WITH ARDS"** exist in the Department of Critical Care Medicine, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate himself/herself under our supervision and guidance.

Supervisor

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APPROVAL PROFORMA
BY RESEARCH & ETHICAL COMMITTEE
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Department	Critical Care Medicine
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Likely date of appearing in PG examination	MAY, 2022
Date of enrollment	APRIL 1, 2020 – APRIL 1 2021
Name of Head of Department	Dr. Parshotam Lal Gautam
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2) Co-Supervisor(s)	Dr. Gunchan Paul
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Jaspal Singh (Professor & Head, Surgery)	Mr. A K Jindal (Member, Ethics Committee)
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PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	Dr. M. RAVI KRISHNA
2	NAME OF THE INSTITUTE	DAYANAND MEDICAL COLLEGE AND HOSPITAL LUDHIANA
3	COURSE OF STUDY AND SUBJECT	D.M. CRITICAL CARE MEDICINE
4	DATE OF ADMISSION OF COURSE	11th SEPTEMBER
5	TITLE OF THE TOPIC	COMPARATIVE EVALUATION OF TRANSPULMONARY PRESSURE GUIDED VENTILATION VERSUS CONVENTIONAL VENTILATION IN PATIENTS WITH ARDS

6 BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Since ARDS net study in 2000 ventilator management for patients with acute respiratory distress syndrome (ARDS) was mainly low tidal volume and high PEEP with maintenance of low plateau pressures. Although low tidal volume ventilation with low plateau pressures appears to be beneficial and lung protective, optimal management of positive end-expiratory pressure (PEEP) was uncertain especially in the setting of altered chest wall compliance conditions like obesity, ascites etc. Higher levels of PEEP have been shown to be protective in numerous animal experiments but have only shown equivocal benefit in human clinical trials.

Lung inflation reflects transpulmonary pressure (P_{TP}), the difference between pressures at the airway opening and the pleural space (P_{TP}=airway pressure−pleural pressure). This would be a satisfactory strategy if pleural pressure values were predictable or restricted to a narrow range. However, there is evidence that pleural pressure varies widely and unpredictably among patients with ARDS, likely due to factors such as obesity, abdominal fluid accumulation and oedema, which influence the mechanical behavior of the chest wall and diaphragm.

Recent trials have shown that mortality has correlation more with driving pressure rather than PEEP. We hypothesize that TPP guided PEEP while improving oxygenation and respiratory mechanics minimizes complication rates. Thus we propose this study to test the effects of transpulmonary pressure guided ventilation on oxygenation, CO_2 exchange and also respiratory mechanics and also whether maintaining low driving pressure results in low VILI events as shown in other trials.[1]

6.2 REVIEW OF LITERATURE

ARDS is a highly heterogeneous life-threatening severe form of acute respiratory failure. It is characterized by an acute onset of hypoxemia refractory to oxygen treatment and the presence of bilateral pulmonary infiltrates on chest radiograph; without mechanical ventilation most patients would die. The mortality rate from acute lung injury and the acute respiratory distress syndrome is approximately 24 to 60 percent depending on age.[2]

Since its first description in 1967[3], there have been a large number of studies addressing various clinical aspects of the syndrome (risk factors, epidemiology, treatment) as well as studies addressing its pathogenesis (underlying mechanisms, biomarkers, genetic predisposition). However, despite this intense research activity, there are very few effective therapies for ARDS other than the use of lung protection strategies.

THE BERLIN DEFINITION OF ACUTE RESPIRATORY DISTRESS SYNDROME[4]

TIMING:	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
CHEST IMAGING:	Bilateral opacities — not fully explained by effusions, lobar/lung collapse, or nodules
ORIGIN OF EDEMA:	Respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present
OXYGENATION	
Mild:	200 mmHg < PaO_2/FIO_2 ≤300 mmHg with PEEP or CPAP ≥5 cmH_2O[c]
Moderate:	100 mmHg < PaO_2/FIO_2 ≤200 mmHg with PEEP ≥5 cmH_2O
Severe:	PaO_2/FIO_2 ≤100 mmHg with PEEP ≥5 cmH_2O

Current therapies

Numerous clinical studies have been conducted in patients with ARDS, but great advances in the care of the patients are still lacking and supportive therapies remain the mainstay in the ARDS management.

Protective mechanical ventilation:

There is a large body of evidence from experimental and clinical studies demonstrating that mechanical ventilation, particularly in the setting of lung injury, can exacerbate functional and structural alterations in the lung.[5] It is noteworthy that mechanical ventilation not only perpetuates lung injury, but also contributes to both the morbidity and mortality of ARDS.[6] The concept that the limitation of end inspiratory lung stretch may reduce mortality in ARDS patients, culminated in the NIH-sponsored multicenter study of patients with ARDS. In this trial, patients randomized to receive a lower tidal volume (Vt) [4-6 mL/kg predict body weight (PBW), and maintenance of plateau pressure between 25 and 30 cmH2O] had a survival benefit. Mortality was reduced from 40% in the conventional arm to 31% in the low Vt arm (CI, 2.4-15.3% difference between groups).[7]

The benefit in terms of mortality and ventilation free days did not appear to be related to the value of the lung compliance at baseline or to the underlying risk factor for ARDS.[8] Of note, the survival benefit was associated with a reduction of plasma IL-6 concentration, supporting the hypothesis that a lung protective strategy limits the spill over into the systemic circulation of inflammatory mediators, which in turn may induce multiple system organ failure.[6]

In addition to lung over-distention, cyclic opening and closing of small airways and alveolar units (so called atelectrauma) can also lead to lung injury.[9] Several clinical trials have been conducted in ARDS patients to examine the effects of an "open lung" approach in which the application of recruitment maneuvers and higher levels of PEEP may limit atelectrauma.

In 2008 a French multi-centre randomized control trial (EXPRESS study) addressed the superiority of an open lung approach in which

PEEP was titrated to the highest value possible keeping Plateau pressure <28-30 cms. Of H_2O.[10]

In the control arm, PEEP was set between 5 and 9 cmH2O. In both groups Vt was <6 mL/kg PBW. Patient treated according to the open lung approach had significantly more ventilator free days and organ failure free days; however, hospital, 28-day and 60-day mortality were not different between the study groups, patients. Of note, patients who now would be considered to have moderate to severe lung injury (P/F <200) tended to have lower 28-day mortality in the higher PEEP group compared to patients treated with lower PEEP.

In two randomized studies, Amato et al, and Villar et al. and colleagues examined the effect of a composite strategy that minimized tidal volume, adopted lung recruitment maneuvers, and applied a level of PEEP above the closing pressure of the lung. Although the intervention arms decreased mortality, the studies were criticized due to relatively small sample sizes and relatively high mortality in the control arms. The ARDS Network performed a second large clinical trial comparing lower vs. higher levels of PEEP (the ALVEOLI study, 2011).[11] The trial was stopped early for futility, showing a trend to worse outcome in the higher PEEP arm, although there was an imbalance in patient characteristics at baseline favoring the control arm; the mean age of the higher PEEP arm was higher (54±17 vs. 49±17, P<0.05), the mean PaO2/FiO2 was lower (151±67 vs. 165±77, P<0.05), and there was a trend to higher APACHE III scores, at baseline.

Similar results were obtained in the Canadian Lung Open Ventilation (LOV) clinical trial.[12] The PEEP values were slightly higher compared to those of the previous ALVEOLI study. The conventional arm received levels of PEEP similar to the ARMA study. The study enrolled 985 patients and it failed to demonstrate any difference in mortality in the two groups (36.4% and 40.4% in the treatment and control groups respectively). The use of rescue therapies and death from refractory hypoxemia were less in the LOV - higher PEEP group.

A recent meta-analysis that incorporated trials (from 1996 to January 2010) comparing higher vs. lower levels of PEEP concluded that there

is no difference in mortality applying lower vs. higher levels of PEEP in patients with mild ARDS. However, in the subgroup of patients with severe ARDS, as defined by a PaO2/FiO2 <200, there was e a benefit from higher levels of PEEP.[13]

To minimize ventilator-induced lung injury, most studies have scaled VT to predicted body weight to normalize VT to lung size. However, in patients with ARDS, the proportion of lung available for ventilation is markedly decreased, which is reflected by lower respiratory-system compliance (CRS).[14] Normalizing V_T to C_{RS} and using the ratio as an index indicating the "functional" size of the lung would provide a better predictor of outcomes in patients with ARDS than V_T alone. This ratio, termed the driving pressure ($\Delta P=V_T/C_{RS}$) can be routinely calculated for patients who are not making inspiratory efforts as the plateau pressure minus PEEP.

In trials of mechanical ventilation involving patients with ARDS, in which V_T and PEEP were included as independent variables, the dependent quantity ΔP was the variable that was most strongly associated with survival. The main goal of mechanical ventilation is to achieve adequate oxygenation and ventilation while minimizing Ventilator induced lung injury. Recent evidence also suggested that ergotrauma was the main predictor of Ventilator induced lung injury rather than PEEP.[1] Ergotrauma is dependent on driving pressure. By using ventilator strategies that minimize transpulmonary/ driving pressure the incidence of VILI can be decreased.

6.3 AIMS AND OBJECTIVES OF THE STUDY

- To test that adjusting driving pressure to achieve positive PTP values will lead to improvement in oxygenation and CO2 exchange
- To compare Transpulmonary guided ventilation and conventional ventilatory strategies for improvement in oxygenation.
- To compare Transpulmonary guided ventilation and conventional ventilatory strategies for improvement in CO2 exchange, static compliance, plateau and peak inspiratory pressures.

7.0 MATERIALS AND METHODS

This study is an institutional and prospective study which will be conducted in Dayanand medical college & hospital for a duration of 1 year from April 2020 to April 2021. The protocol will be approved by the institutional ethics board.

7.1 SOURCE OF DATA:

GROUP ALLOCATION:

Patient will be randomly allocated to either of two groups based on computer generated random numbers.

GROUP T: will receive transpulmonary pressure guided ventilation.

GROUP C: will receive conventional ventilation.

7.2 METHOD OF COLLECTION OF DATA

INCLUSION CRITERIA:

- Patients will be included in the study if they have moderate-to-severe ARDS according to the American-European Consensus Conference definitions.[15]
- Duration of ARDS 36 hours or less from meeting final Berlin criterion.
- Age more than 18 years.

EXCLUSION CRITERIA:

- Received mechanical ventilation more than 96 h.
- Recently treated for bleeding varices, stricture, haematemesis, esophageal trauma, recent esophageal surgery or other contraindication for nasogastric tube placement.
- History of lung or liver transplantation.
- Evidence of active air leak from the lung (including bronchopleural fistula, pneumothorax, pneumomediastinum or air leak from existing chest tube).
- Severe chronic liver disease (Child-Pugh Score ≥12).
- Patients not committed to full support.
- Inability to get informed consent from the patient or surrogate.
- Use of rescue therapies prior to enrolment (including nitric oxide, ECMO, prone positioning)

OUTCOME:

Primary outcome:

- Improvement in PaO2 /FiO2 ratio

Secondary outcome:

- Improvement in static compliance
- VILI like spontaneous pneumothorax
- Improvement in CO2 exchange

Measurements and Experimental Protocol

While undergoing treatment, the subjects will be supine, with the head of the bed elevated to 30 degrees. Airway pressure, tidal volumes and other respiratory parameters will be recorded during mechanical ventilation.

An esophageal balloon catheter will be passed to a depth of 60 cms. from the incisors for measurement of gastric pressure and then withdrawn to a depth of 40 cms. to record esophageal pressure during mechanical ventilation. Placement of the balloon in the stomach will be confirmed by a transient increase in pressure during a gentle compression of the abdomen and by a qualitative change in the pressure tracing (i.e., an increased cardiac artifact) as the balloon will be withdrawn into the esophagus.

After these initial measurements, patients will be randomly assigned with the use of a block-randomization scheme to the control or esophageal pressure-guided group. Each patient, while under heavy sedation or paralysis with R.A.S.S. score of 0 to -1, will undergo a recruitment maneuver to standardize the history of lung volume. The patients in the esophageal-pressure-guided group will undergo mechanical ventilation with settings determined by the initial esophageal-pressure measurements. Tidal volume will be set at 6 ml per kilogram of predicted body weight. PEEP levels will be set to achieve a transpulmonary pressure of 0 to 10 cm of water at end expiration, according to a sliding scale based on the partial pressure of arterial oxygen (PaO_2) and the fraction of inspired oxygen. We will also limit tidal volume to keep transpulmonary pressure at less than 25 cms. of water at end inspiration.

Patients in the control group will be treated according to the low-tidal-volume strategy reported by the ARDS Net study of the National Heart, Lung, and Blood Institute.[8] These patients will be ventilated using volume control mode with the tidal volume set at 6 ml per kilogram of predicted body weight and PEEP is based on the patient's PaO_2 and FiO_2.

In both groups, the goals of mechanical ventilation will include a PaO_2 of 55 to 120 mm. of Hg or a pulse-oximeter reading of 88 to 98%, an arterial pH of 7.30 to 7.45, and a partial pressure of arterial carbon dioxide ($PaCO_2$) of 40 to 60 mm Hg.

To reduce the need for frequent manipulation of the ventilator settings, the goals for oxygenation in both groups will be relaxed from the narrow range of PaO_2 values in the ARDS Net study (55 to 80 mm Hg) to a broader range of 55 to 120 mm Hg.

All measurements will be repeated 5 minutes after the initiation of experimental or control ventilation and again at 6 hours.

The primary end point of the study is comparison of arterial oxygenation, as measured by the ratio of PaO2 to FiO_2 (PaO_2:FiO_2) 6 hours after ventilation using either strategies. The secondary end points included indexes of lung mechanics and gas exchange (respiratory system compliance and the ratio of physiological dead space to tidal volume).

STATISTICAL ANALYSIS:

In evaluating the PaO2:FIO2 at 6 hours, we decided a priori that a clinically important change in the PaO2:FIO2 would be approximately 20%, with measurement error taken into account. To determine sample size, we chose a minimal average between-groups difference of 40 in the PaO2:FIO2. We conservatively estimated the standard deviation to be 100 (equivalent to a coefficient of variation of 250%); on the basis of this estimate, a sample of 50 patients per group would be required to detect a difference of 40 in the PaO2:FIO2 with 80% power and a two-tailed alpha value of 0.05.

Continuous variables with normal distribution are presented as means (±SD) and compared with the use of Student's t-test. Continuous

variables with non-normal distributions are presented as medians and interquartile ranges and compared with the use of the Mann–Whitney test. Dichotomous or nominal categorical variables are compared with the use of the chi-square test with normal approximation or Fisher's exact test, as appropriate. A two-tailed P value less than 0.05 was considered to indicate statistical significance. Statistical analysis will be performed using SPSS version 21.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

NO

7.4 HAS ETHICAL CLEARENCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

ATTACHED HEREWITH

8.0 LIST OF REFERENCES

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PROFORMA

Informed consent taken

Name of the Patient

Age: Sex: religion: Ip/Op no.:

Weight: Predicted body weight: height:

Address

Religion

Occupation

Chief complaints: Fever

Cough with Expectoration

Chest pain

Past history

COPD, CLD, Chronic kidney disease, Diabetes mellitus, hypertension or any other comorbities

Family history

Personal history: Diet

Sleep

Appetite

Bowel & Bladder habits

Addictions

Signature of Candidate **Signature of Supervisor**

General examination

Built and Nourishment

Pallor	Cyanosis	Clubbing
Icterus	Edema	Lymphadenopathy
Vitals:	Temperature	Pulse
	Blood Pressure	Respiratory Rate
	Saturation	

Systemic Examination

Respiratory System:

Cardiovascular system

Abdomen

Nervous system

MEASUREMENTS:

Duration of mechanical ventilation prior to trial:

Signature of Candidate

Signature of Supervisor

VENTILATION PARAMETERS:

PARAMETER	BASELINE VALUE	AT 6 HOURS	AT 12 HOURS
PEEP			
Peak inspiratory pressure			
Tidal volume			
Respiratory rate			
Plateau pressure			
Mean airway pressure			
Ti (seconds)			
PEEPt (total peep)			
Pes (end-expiratory hold)			
Ptp (end-expiratory hold)			
Pes (end-inspiratory hold)			
Ptp (end-inspiratory hold)			
Mixed expired CO2			

ARTERIAL BLOOD ANALYSIS

	BASELINE	AT 6 HOURS	AT 12 HOURS
pH			
PaCO2			
PaO2			
HCO3			
Base excess			

Signature of Candidate **Signature of Supervisor**

DRUG USE

Vasoactive drugs, dose

DRUGS	DOSE

Continuous sedative or paralytic drugs, dose:

DRUGS	DOSE

Cumulative fluid balance:

24 hours fluid balance:

Laboratory Examination

Complete Blood Picture

Chest X ray PA view

Blood Urea

Serum Creatinine, USG abdomen, Serum calcium, Serum electrolytes

Liver function tests

ECG, 2D echocardiography

Signature of Candidate **Signature of Supervisor**

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o.....
.....am willing to participate in the study **"COMPARATIVE EVALUATION OF TRANSPULMONARY PRESSURE GUIDED VENTILATION VERSUS CONVENTIONAL VENTILATION IN PATIENTS WITH ARDS"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

.....
Signature of the Witness

.....
Signature of the patient

Name:

Signature of Candidate

Signature of Supervisor

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य **"COMPARATIVE EVALUATION OF TRANSPULMONARY PRESSURE GUIDED VENTILATION VERSUS CONVENTIONAL VENTILATION IN PATIENTS WITH ARDS"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

"COMPARATIVE EVALUATION OF TRANSPULMONARY PRESSURE GUIDED VENTILATION VERSUS CONVENTIONAL VENTILATION IN PATIENTS WITH ARDS" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ